Volume 2

EFFECT OF RADIATION ON HUMAN HEALTH

Radiation Health Effects of Medical and Diagnostic X-Rays

HEARINGS

BEFORE THE

SUBCOMMITTEE ON
HEALTH AND THE ENVIRONMENT

OF THE

COMMITTEE ON
INTERSTATE AND FOREIGN COMMERCE
HOUSE OF REPRESENTATIVES

NINETY-FIFTH CONGRESS

SECOND SESSION

ON

CONCERN ABOUT THE OVER USE OF X-RAYS, THE POTENTIAL HEALTH HAZARDS POSED BY X-RAYS AND THE EXISTING LEVELS OF X-RAY EXPOSURES WHICH WE NOW CONSIDER SAFE

JULY 11, 12, 13, AND 14, 1978

Serial No. 95–180

Printed for use of the
Committee on Interstate and Foreign Commerce

U.S. GOVERNMENT PRINTING OFFICE
36-120 O WASHINGTON : 1979

For sale by the Superintendent of Documents, U.S. Government Printing Office
Washington, D.C. 20402

H 501-59

COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE

HARLEY O. STAGGERS, West Virginia, *Chairman*

JOHN E. MOSS, California
JOHN D. DINGELL, Michigan
PAUL G. ROGERS, Florida
LIONEL VAN DEERLIN, California
FRED B. ROONEY, Pennsylvania
JOHN M. MURPHY, New York
DAVID E. SATTERFIELD III, Virginia
BOB ECKHARDT, Texas
RICHARDSON PREYER, North Carolina
CHARLES J. CARNEY, Ohio
RALPH H. METCALFE, Illinois
JAMES H. SCHEUER, New York
RICHARD L. OTTINGER, New York
HENRY A. WAXMAN, California
ROBERT (BOB) KRUEGER, Texas
TIMOTHY E. WIRTH, Colorado
PHILIP R. SHARP, Indiana
JAMES J. FLORIO, New Jersey
ANTHONY TOBY MOFFETT, Connecticut
JIM SANTINI, Nevada
ANDREW MAGUIRE, New Jersey
MARTY RUSSO, Illinois
EDWARD J. MARKEY, Massachusetts
THOMAS A. LUKEN, Ohio
DOUG WALGREN, Pennsylvania
BOB GAMMAGE, Texas
ALBERT GORE, Jr., Tennessee
BARBARA A. MIKULSKI, Maryland

SAMUEL L. DEVINE, Ohio
JAMES T. BROYHILL, North Carolina
TIM LEE CARTER, Kentucky
CLARENCE J. BROWN, Ohio
JOE SKUBITZ, Kansas
JAMES M. COLLINS, Texas
LOUIS FREY, Jr., Florida
NORMAN F. LENT, New York
EDWARD R. MADIGAN, Illinois
CARLOS J. MOORHEAD, California
MATTHEW J. RINALDO, New Jersey
W. HENSON MOORE, Louisiana
DAVE STOCKMAN, Michigan
MARC L. MARKS, Pennsylvania

W. E. Williamson, *Chief Clerk and Staff Director*
Kenneth J. Painter, *First Assistant Clerk*
Eleanor A. Dinkins, *Assistant Clerk*
William L. Burns, *Printing Editor*

Subcommittee on Health and the Environment

PAUL G. ROGERS, Florida, *Chairman*

DAVID E. SATTERFIELD III, Virginia
RICHARDSON PREYER, North Carolina
JAMES H. SCHEUER, New York
HENRY A. WAXMAN, California
JAMES J. FLORIO, New Jersey
ANDREW MAGUIRE, New Jersey
EDWARD J. MARKEY, Massachusetts
RICHARD L. OTTINGER, New York
DOUG WALGREN, Pennsylvania
HARLEY O. STAGGERS, West Virginia (Ex Officio)

TIM LEE CARTER, Kentucky
JAMES T. BROYHILL, North Carolina
EDWARD R. MADIGAN, Illinois
JOE SKUBITZ, Kansas
SAMUEL L. DEVINE, Ohio (Ex Officio)

Stephen E. Lawton, *Counsel*
Robert W. Maher, *Director of Research and Planning*
Jo Anne Glisson, *Senior Staff Associate*
Donald W. Dalrymple, *Assistant Counsel*

CONTENTS

Page

Hearings held on—

July 11, 1978 1
July 12, 1978 193
July 13, 1978 543
July 14, 1978 693

Statement of—

Bailar, John C. III, M.D., Ph. D., Washington, D.C 1032
Bertell, Rosalie, Ph. D., GNSH, Buffalo, N.Y 3, 74
Boice, John D., Jr., Ph. D., Environmental Epidemiology Branch, Division of Cancer Cause and Prevention, National Cancer Institute, National Institutes of Health, Public Health Service, Department of Health, Education, and Welfare 693
Caldwell, George, on behalf of American Hospital Association 672
Cooper, Richard M., Chief Counsel, Food and Drug Administration, Public Health Service, Department of Health, Education, and Welfare 194
Costlow, Richard D., Ph. D., Division of Cancer Control and Rehabilitation, National Cancer Institute, National Institutes of Health, Public Health Service, Department of Health, Education, and Welfare 693
Dolezal, Alice, chairwoman, Conference of Radiation Control Program Directors 543
Gehrig, Leo J., M.D., senior vice president, American Hospital Association . 672
Goepp, Robert, D.D.S., member, council on dental research, American Dental Association 623
Gowen, Richard J., Ph. D., member, board of directors, Institute of Electrical and Electronic Engineers, Inc 1142
Hevezi, James, Ph. D., on behalf of Institute of Electrical and Electronic Engineers, Inc 1142
Kennedy, Donald, Ph. D., Commissioner, Food and Drug Administration, Public Health Service, Department of Health, Education, and Welfare .. 194
Kushner, Rose, executive director, Breast Cancer Advisory Center 3, 153
Laws, Priscilla W., Ph. D., associate professor of physics, Dickinson College . 3, 9
Linton, Otha W., M.S.J., director of Government relations, American College of Radiology 49
McClenahan, John L., M.D., Philadelphia, Pa 3, 54
McCune, Robert G., division staff manager, radiological imaging products division, National Electrical Manufacturers Association 1197
Martin, James E., Ph. D., Deputy Director, Criteria and Standards Division, Office of Radiation Programs, Environmental Protection Agency ... 1115
Morgan, Russell H., M.D., on behalf of American College of Radiology 491
Nelson, Devaughn R., Federal Guidance Branch, Division of Criteria and Standards, Office of Radiation Programs, Environmental Protection Agency 1115
Phillips, Leon A., M.D., associate professor of radiology, University of Washington 3
Pomerance, William, M.D., Division of Cancer Biology and Diagnosis, National Cancer Institute, National Institutes of Health, Public Health Service, Department of Health, Education, and Welfare 693
Reiskin, Allan B., D.D.S., professor of radiology, department of oral diagnosis, school of dental medicine, University of Connecticut 3, 57
Rowe, William D., Ph. D., Deputy Assistant Administrator for Radiation Programs, Environmental Protection Agency 1115
Stanford, John W., D.D.S., secretary, council on dental materials and devices, American Dental Association 623

Page

Suttle, Thomas, Institute of Electrical and Electronic Engineers, Inc. (Washington office) ... 1142

Upton, Arthur C., M.D., Director, National Cancer Institute, National Institutes of Health, Public Health Service, Department of Health, Education, and Welfare ... 693, 1105

Villforth, John C., Director, Bureau of Radiological Health, Food and Drug Administration, Public Health Service, Department of Health, Education, and Welfare ... 194

Wener, Louis, M.D., on behalf of American Hospital Association ... 672

Wyckoff, Harold O., Ph. D., president, international commission on radiation units and measurements, American College of Radiology ... 491

Additional material submitted for the record by—

- American College of Radiology, attachment to Dr. Morgan's prepared statement, "Federal Government's Impact on Radiology," the ... 531
- American Dental Association:
  - ADA position to third party requirements ... 644
  - Letter, dated August 8, 1978 from John Stanford to Chairman Rogers, re list of consultants in the area of radiology ... 634
  - Letter, dated August 10, 1978 from Robert Goepp to Chairman Rogers, re critique of the Pennsylvania Blue Shield Study ... 668
  - Past and current projects with costs involved ... 637
  - Quality assurance in dentistry ... 650
  - Routine full mouth radiographic examinations ... 643
- Bailar, John C., III, M.D., Ph. D., attachments to prepared statement:
  - Attachment 1—International symposium on the late biological effects of ionizing radiation ... 1052
  - Attachment 2—Breast cancer detection demonstration units ... 1060
  - Attachment 3—Letter dated March 30, 1973 from Kenneth B. Olson, M.D ... 1065
  - Attachment 4—Screening for early breast cancer: pros and cons ... 1066
  - Attachment 5—Comments on the national breast cancer demonstration project ... 1079
  - Attachment 6—Breast cancer demonstration project ... 1089
  - Attachment 7—Comments on breast cancer screening ... 1093
  - Attachment 8—Letter dated June 30, 1973 from Dr. Lee to Dr. Bailar re comments on breast cancer detection demonstration project ... 1097
  - Evaluation of breast cancer demonstration projects ... 1112
- Bertell, Rosalie, Ph. D., GNSH, attachment to prepared statement, and responses to questions:
  - Responses to questions on medical and dental diagnostic X-ray ... 184
  - X-ray exposure and premature aging ... 140
- Conference of Radiation Control Program Directors, attachments to Ms. Dolezal's prepared statement:
  - Healing arts X-ray control program criteria ... 549
  - Letter, dated May 15, 1978 from Ms. Dolezal to Senators Ribicoff and Glenn re views on organizational issues concerning Federal radiation health and safety programs ... 565
  - Rules and regulations of Minnesota Department of Health ... 573
- Environmental Protection Agency, attachment to Dr. Rowe's prepared statement, excerpt from the Federal Register—Radiation protection guidance to Federal agencies for diagnostic X-rays ... 1135
- Health, Education, and Welfare Department:
  - A Look at FDS's Program to Protect the American Consumer from Radiation, April 1977, by Bureau of Radiological Health ... 196
  - Assessment of the health effects from unnecessary X-ray examinations ... 295
  - Breast exposure: nationwide trends (BENT) ... 948
  - Clarification of the two radiologist studies ... 301
  - Contract research summary ... 702
  - Correspondence and related materials opposing the tightening of guidelines by American Cancer Society ... 950
  - Difficulties under the Privacy Act ... 907
  - Efforts to extend the President's medical radiation recommendations to the private sector ... 332
  - Enforcement of the diagnostic X-ray performance standard under the radiation control for Health and Safety Act of 1968 ... 401

Page
Estimated risks of radiation-induced cancer, attachment of Dr. Upton's prepared statement 699
FDA assessment of the Bross and Bertell work, an 48
FDA radiological health personnel trends 438
Federal Government's impact on radiology 531
Federal implementation of the Presidential directive regarding medical radiation guidance 324
Fiscal year 1978—FDA radiological health program resources 439
Health effects of low-level radiation 910
Impact of Presidential directive on medical radiation guidance 322
Ionizing research—1980 464
Modification No. 2 to the screening guidelines for the BCDDP 933
NCI grant project summary 791
National Institutes of Health interagency agreement 915
NIH policy on employee X-ray examinations 320
Nonionizing research—1980 464
PHS commissioned corps policy on pre-employment chest X-ray examinations 320
Proposed new and expanded legislative authorities under Public Law 90-602 481
Radiation registry of physicians 303
Radiogenic cancer studies—medical exposure 911
Reasonable State X-ray equipment inspection program 489
Results of the original thyrotoxicosis study and the new extension 435
Summary of current chest X-ray practices and policies among Federal hospitals/agencies 326
Summary of experimental and epidemiological research on ionizing radiation biological effects 223
Summary of FDA activities to reduce unnecessary medical radiation exposure of the human embryo and fetus 335
Summary of FDA/BRH active grants 441
Summary of FDA/BRH active research contracts and interagency agreements 466
Summary of problems related to lasers and nonserious use of laser devices 431
X-rays and pregnancy 398
Institute of Electrical and Electronic Engineers, Inc.:
Appendix I—Computed tomography 1163
Appendix II—Electronics in medicine 1166
Appendix III—Diagnostic ultrasound 1171
Responses to questions by the subcommittee 1179
Laws, Priscilla W., Ph. D., attachments to prepared statement:
References 20
Chapter 12—How X-rays affect people 23
Chapter 13—Risks associated with X-ray diagnosis 31
Appendix A—Units of radiation exposure and dose 42
Appendix B—Exposures to embryo and fetus 45
Appendix C—Average doses for typical X-ray examinations in millirads 50
Appendix D—Personal radiation record—diagnostic X-rays 53
National Electrical Manufacturers Association, attachment to Mr. McCune's prepared statement, letter to Chairman Rogers, re increased radiological equipment cost over the past 5 years 1213
Phillips, Leon A., M.D., attachment to prepared statement, request form for skull radiography 7
Reiskin, Allan B., D.D.S., professor of radiology, department of oral diagnosis, school of dental medicine, University of Connecticut, subsequent letter to Chairman Rogers re need for legislation to prevent the sale of X-ray machines to unqualified users and the desirability of establishing minimum educational requirements. 190
Statements submitted for the record by—
American Society of Radiologic Technologists 1221
Xonics Inc 1231
Letter submitted for the record by—
Blue Cross Association, National Association of Blue Shield Plans, Walter J. McNerney, president 1235

ORGANIZATIONS REPRESENTED AT HEARINGS

American College of Radiology:
  Linton, Otha, A., M.S.J., director of government relations.
  Morgan, Russell H., M.D., on behalf of.
  Wyckoff, Harold O., Ph. D., president, international commission of radiation and measurements.
American Dental Association:
  Goepp, Robert, D.D.S., member, council on dental research.
  Stanford, John, D.D.S., secretary, council on dental materials and devices.
American Hospital Association:
  Caldwell, George, on behalf of.
  Gehrig, Leo J., M.D., senior vice president.
  Wener, Louis, M.D., on behalf of.
Breast Cancer Advisory Center, Rose Kushner, executive director.
  Conference of Radiation Control Program Directors, Alice Dolezal, chairwoman.
Environmental Protection Agency:
  Martin, James E., Deputy Director, Criteria and Standards Division, Office of Radiation Programs.
  Nelson, Devaughn R., Federal Guidance Branch, Division of Criteria and Standards, Office of Radiation Programs.
  Rowe, William D., Ph. D., Deputy Assistant Administrator for Radiation Programs.
Health, Education, and Welfare Department:
  Boice, John D., Jr., Ph. D., Environmental Epidemiology Branch, Division of Cancer Cause and Prevention, National Cancer Institute, National Institutes of Health, Public Health Service.
  Cooper, Richard M., Chief Counsel, Food and Drug Administration, Public Health Service.
  Costlow, Richard D., Ph. D., Division of Cancer Control and Rehabilitation, National Cancer Institute, National Institutes of Health, Public Health Service.
  Kennedy, Donald, Ph. D., Commissioner, Food and Drug Administration, Public Health Service.
  Pomerance, William, M.D., Division of Cancer Biology and Diagnosis, National Cancer Institute, National Cancer Institutes of Health, Public Health Service.
  Upton, Arthur C., M.D., Director, National Cancer Institute, National Institutes of Health, Public Health Service.
  Villforth, John C., Director, Bureau of Radiological Health, Food and Drug Administration, Public Health Service.
Institute of Electrical and Electronic Engineers, Inc.:
  Gowen, Richard J., Ph. D., member, board of directors.
  Hevezi, James, Ph. D., on behalf of.
  Shuttle, Thomas (Washington office).
National Electrical Manufacturers Association, Robert G. McCune, division staff manager, radiological imaging products division.

EFFECT OF RADIATION ON HUMAN HEALTH

Radiation Health Effects of Medical and Diagnostic X-Rays

TUESDAY, JULY 11, 1978

House of Representatives,
Subcommittee on Health and the Environment,
Committee on Interstate and Foreign Commerce,
Washington, D.C.

The subcommittee met, pursuant to notice, at 2:16 p.m. in room 2322, Rayburn House Office Building, Hon. Paul G. Rogers, chairman, presiding.

Mr. Rogers. The subcommittee will come to order, please.

Today's hearings are a continuation of the committee's oversight into the effects of radiation on human health.[1] This set of hearings, which will continue through this week, will address the area of medical and dental diagnostic X-rays.

We began these hearings earlier this year by looking into the atomic bomb tests of the 1950's and 1960's and this was rather dramatic indeed. There may have been one-half million people involved with these tests.

By comparison, there are an estimated 240 million X-ray procedures ordered each year by medical and dental practitioners. This represents nearly 90 percent of the manmade radiation to which the general public is exposed.

Because this is manmade radiation it can be controlled. I am unaware of any movement which would have us turn away from the use of X-rays. The benefits of X-rays are well documented.

There is concern, however, about the over use of X-rays, the potential health hazards posed by X-rays, and the existing levels of X-ray exposures which we now consider safe.

The overutilization of X-rays for diagnostic purposes alone is estimated to cost the public $2 billion a year. This cost implication is quite aside from the health implications which some men and women of science have told us are not being properly addressed.

Our witnesses today are scientists, practitioners, and consumers who share a common bond—that being a concern over medical and dental use of X-rays for diagnostic purposes.

There have been estimates that 7 out of every 10 Americans receive X-rays each year. If we do have a potential health problem with X-rays, then I think that these figures express vividly the scope of the problem.

---

[1] Volume 1, "Effect of Radiation on Human Health, Health Effects of Ionizing Radiation," held January 24, 25, 26, February 8, 9, 14, and 28, 1978, Serial No. 95-179.

Dr. Carter may have a statement.

Mr. CARTER. Thank you, Mr. Chairman. I am pleased to join you in holding hearings this week on the topic of medical and dental diagnostic X-rays as part of our subcommittee's work on the health effects of low-level radiation.

As a physician, I am particularly aware of the lifesaving potential of diagnostic and therapeutic radiology, as well as the possible health risks associated with exposure to ionizing radiation.

We know that in order to make an informed judgment about whether or not to use X-ray techniques, there must be a weighing of the known risks and benefits to the patient. And, of course, the sophistication of that judgment depends on the nature of the scientific and medical knowledge available at that time.

Over the years we have seen how dramatically that knowledge and medical practice have changed.

For example, in the past, radiation treatment was relatively commonplace and X-rays were used for a variety of conditions from ringworm of the scalp to tuberculosis. Also, children with thymus enlargement or swollen tonsils or acne were given therapeutic doses of X-rays. Nowadays, we realize that these procedures are not advisable, particularly in light of alternative treatment procedures. Yet in the past they were considered acceptable.

Therefore, it is essential that we base our decisions about the use of X-rays on the best available information regarding benefits and risks to the particular patient. Our subcommittee's previous hearings have increased our awareness about the potential risks of very low levels of radiation, and certainly we must not take its medical application lightly. I doubt that any physician or dentist does.

Clearly, we must do all that we can to insure that patients are not exposed to unnecessary X-ray procedures or to faulty equipment. Personnel who administer X-rays should be well trained in the use of these techniques and knowledgeable about safety precautions.

Yet we must not refrain from using diagnostic and therapeutic radiology simply because there are risks involved. There are risks associated with just about everything we do. What we must do is make the best possible judgment, in light of current knowledge, about the risks and benefits of X-ray for a particular patient. And we must continue to seek the information necessary to make the best possible decisions for our patients and the public health in general.

Thank you, Mr. Chairman.

Mr. ROGERS. Thank you.

Our panel today will be composed of—and if they would like to take seats at the witness table as I call their names, the committee would appreciate it—Dr. Rosalie Bertell, Buffalo, N.Y.

Is Dr. Bertell here?

We welcome you. If you would like to take a chair.

Is Dr. Priscilla Laws here yet?

Dr. Laws, we welcome you; associate professor of physics, Dickinson College, Carlisle, Pa.

Dr. John L. McClenahan, who is a practicing radiologist. Doctor, we welcome you.

Dr. Leon Phillips, the associate professor of radiology, University of Washington, University Hospital of Seattle. Dr. Phillips, we are pleased to have you with us.

Dr. Allan B. Reiskin, who is professor and chief of radiology, Department of Oral Diagnosis, Division of Oral Radiology, University of Connecticut, School of Dental Medicine.

Rose Kushner, who is director of the Breast Cancer Advisory Center in Kensington, Md.

The committee welcomes each of you to the hearings. We wish to express to you the committee's appreciation for your willingness to appear this afternoon and to help us with your expert advice on this subject matter. Your statements will be made a part of the record in full.

Perhaps we will start with Dr. Phillips.

STATEMENTS OF LEON A. PHILLIPS, M.D., ASSOCIATE PROFESSOR OF RADIOLOGY, UNIVERSITY OF WASHINGTON; PRISCILLA W. LAWS, PH. D., ASSOCIATE PROFESSOR OF PHYSICS, DICKINSON COLLEGE; JOHN L. McCLENAHAN, M.D., PHILADELPHIA, PA.; ALLAN B. REISKIN, D.D.S., PROFESSOR OF RADIOLOGY, DEPARTMENT OF ORAL DIAGNOSIS, SCHOOL OF DENTAL MEDICINE, UNIVERSITY OF CONNECTICUT; ROSALIE BERTELL, PH. D., GNSH, BUFFALO, N.Y.; AND ROSE KUSHNER, EXECUTIVE DIRECTOR, BREAST CANCER ADVISORY CENTER

Dr. PHILLIPS. Thank you, Chairman Rogers, Dr. Carter, and guests.

As an academic radiologist for 22 years, I have long been aware of several areas in diagnostic radiology where the contribution to patient care is questionable in relation to the expense involved and the patient radiation received. I would like to share with you today some experiences and data gathered in utilization review projects performed at two Seattle hospitals. The projects involve two diagnostic radiographic procedures which are peformed by most hospitals in the United States: skull radiography and X-ray pelvimetry.

All radiologists will admit that there is an extremely low information yield in radiography of the skull. This was documented by a 3-month sampling back in 1967 at Harborview Medical Center in Seattle, which revealed that only 1 skull examination out of every 41 actually made a significant contribution to patient care. A prospective study was therefore designed and performed by Drs. Bell and Loop of the University of Washington Department of Radiology in 1969-70 utilizing a hypothesized high yield criteria list indicating the need for skull radiography in trauma. This study identified 93 skull fractures in 1,500 skull examinations, and only 1 of these would not have been detected had the high yield criteria been applied, while 434 examinations would not have been done. At this time it was suggested that the high yield criteria might save $15 million a year in health care costs nationally.

In 1973, the Utilization Review Committee of the University Hospital reviewed the foregoing report and recommended implementation of the high yield criteria list in its emergency room. This proposal was opposed by the Department of Neurosurgery, and a policy was promulgated which stated that all patients presenting with a history of/or clinical signs of skull trauma would be seen by a member of the Department of Neurosurgery who would make the decision as to the need for skull radiography. The Utilization Review Committee monitored this policy, documenting the inability of the neurosurgeon staff to meet this commitment and compared the indications used for skull radiography against the criteria list that had been proposed. A monthly summary of this activity was prepared and circulated to all physicians able to request this examination from the emergency facility. This monitoring effort produced the following results:

Skull radiography decreased 39 percent in the emergency facility;

All significant positive results were identified by the high yield criteria list;

If the high yield criteria list had been used, the number of skull examinations would have been reduced 80 percent.

In 1974, a medical staff ad hoc committee reviewed the collected data and agreed upon a modified high yield criteria, with only 13 criteria now, which became a part of a new policy on emergency facility skull radiography. This policy encouraged voluntary compliance with the high yield criteria list, and the Utilization Review Committee continued its monitoring efforts. Once again, there were no significant positive reports identified for other than the high yield criteria and the compliance rate remained at only about 50 percent.

During the academic year 1975–76, the Bureau of Radiologic Health of the Food and Drug Administration supported a project comparing the utilization pattern at Harborview Medical Center where there was no policy or other constraints for requesting skull radiography to that of the University Hospital with a defined policy containing a high yield criteria list. Retrospective reviews of the radiology reports and the patients' charts were made 6 to 8 months following the performance of the examinations in all cases receiving a positive report and including all cases with high yield criteria indicated at the University Hospital facility.

At Harborview Medical Center there were 2,275 skull examinations which were made, which represented an increase of 60 percent since the 1972–73 academic year. At the University Hospital, only 258 examinations were made, representing a decrease of 40 percent since the 1972–73 academic year. The ratio of significant positive reports to total examinations was 1 in 44 at Harborview and 1 in 28 at the University Hospital. Once again, at both facilities there were no significant positive reports made for patients that did not have one of the high yield criteria identified.

A current project being conducted as an ancillary services demonstration project for the Washington State Professional Standards Review Organization and supported by the Bureau of Radiologic Health involves implementation of a high yield criteria list now containing only nine criteria at both the Harborview Medical Center and the University Hospital. After 9 months, a 31 percent reduction in skull radiography has been recorded at Harborview and a further reduction to 60 percent of the premonitoring rate at the University Hospital. If full compliance with the criteria list had been achieved, there would have been a decrease of more than 80 percent at both institutions.

Why has voluntary compliance with the high yield criteria list averaged only 50 to 60 percent? The answer to this lies in the fact that the overall community standard remains that of routine filming of all head trauma cases, and physicians are afraid that if they don't make skull films, they may be inviting malpractice activity.

A thorough review of the literature and the experience of malpractice insurers indicates that physicians are much more likely to be sued for missed diagnosis after obtaining skull films than for not making them at all. Indeed, unwarranted reliance on a negative skull examination appears to be the cause of most malpractice suits involving skull films. An excellent example of this is a record malpractice award of over $4 million made in a San Francisco court when unwarranted reliance on a false negative skull radiographic examination contributed to inadequate patient examination and subsequent inadequate observation with resulting extensive paralysis of a 13-year-old boy. Skull radiography actually appears to increase a physician's legal jeopardy. When this fact becomes more generally appreciated, physicians will not insist upon making routine skull examinations in emergency rooms.

A review protocol has been designed for auditing skull radiography in nonteaching hospitals in the State of Washington and ultimately, for use of PSRO's in other States.

A revealing speculation as to the potential impact of controlling the utilization of skull radiography in the United States can be appreciated by examining a few brief statistics:

The number of skull radiographic examinations performed in the United States in 1970 was 4,220,000.

The number of skull radiographic examinations made in the United States in 1978—this assumes a 50 percent utilization increase—the total in 1978 would be approximately 6,330.000.

The average cost of skull radiography today is $50, and the probable total value of skull radiography in the United States in 1978 is $316,500,000.

Our studies suggest that this figure can be reduced quite easily to 50 percent and, with good adherence to a high yield criteria list, to a possible 80 percent, without adverse effect to patient care.

Now, a second area of suspected malutilization of the ancillary service of diagnostic radiology is X-ray pelvimetry. this area is more important for the excessive radiation involved rather than for the costs. It is now the greatest single source of fetal irradiation. Even though this irradiation is still considered a low dose level—and I think the fetus gets about 700 to 800 milliroentgens with this examination—most experts now agree that there is an increased incidence of leukemia and other childhood malignancies at these dosage levels.

A review of the current literature in regard to the utility of X-ray pelvimetry suggests that this procedure is relatively useless in predicting difficulties in the outcome of labor. A comprehensive study of 67,000 single deliveries from 16 training institutions made in 1975 included an evaluation of over 4,500 pelvimetries in which the following observations were made:

There were no consistent factors or combination of factors which indicated the need for pelvimetry.

There was no consistent relationship between pelvimetry and the cesarean section rates at the hospitals in the study.

Pelvimetry did not significantly shorten labor in those women with cephalopelvic disproportion when compared to the use of clinical judgment alone.

The mean and median labor lengths for women with pelvimetry, were about 2 hours longer than those without pelvimetry.

It would appear that the only remaining role for X-ray pelvimetry is in the management of a breech presentation if vaginal delivery is contemplated.

At the University of Washington Hospital, we make approximately 100 to 200 pelvimetries each year, mostly by insecure residents in training seeking assurance and believing that it was necessary to avoid litigation activity. When this utilization pattern was discussed with senior members of the Department of Obstetrics, in the light of growing literature on radiation hazards and utilization of X-ray pelvimetry, a policy was promulgated which required all X-ray pelvimetry to be approved by a senior staff physician. this policy has all but eliminated X-ray pelvimetry as a source of fetal radiation at the University Hospital; there have been only two poorly indicated studies performed in the last 7 months. When they were examined these were ones they failed to screen; they sneaked through.

The weight of evidence against X-ray pelvimetry is now such that the time has come for it to be drastically curtailed. The Washington State Professional Standards Review Organization is now proceeding to evaluate the utilization pattern and to educate physicians concerning the use of X-ray pelvimetry in hopes of spreading the results observed at the University Hospital to the rest of the State of Washington.

In summary, I would like to make the following three statements. The concurrent implementation of a high yield criteria list has reduced skull radiography more than 30 percent at Harborview Medical Center and more than 60 percent at the University Hospital. Outcome analyses by retrospective chart reviews reveal that skull radiography can be reduced by as much as 80 percent without adverse effect upon patient care, and X-ray pelvimetry can probably be abandoned, except for possible use in breech presentation with anticipated vaginal delivery.

Thank you very much.

[Attachment to Dr. Phillips prepared statement follows:]

Skull Radiography Policy
for
Emergency Facilities of
Harborview Medical Center
and
University of Washington Hospital

THIS FORM MUST ACCOMPANY ALL REQUESTS FOR SKULL RADIOGRAPHY.

All patient's presenting to these emergency facilities should have a careful clinical evaluation prior to requesting skull radiography. The following clinical situations should have skull radiography without fail. If any other clinical reason for requesting skull films exists, please list under (10) Other ----.

☐ 1. Unconsciousness (including unarousable alcoholic) at time of presentation to emergency facility.

☐ 2. Documented decreasing level of consciousness or progressive mental deterioration.

☐ 3. History of previous craniotomy with shunting tube in place.

☐ 4. Skull depression or subcutaneous foreign body palpable or identified by probe through laceration or puncture wound.

☐ 5. Hemotympanum or fluid discharge from ear.

☐ 6. C.S.F. discharge from nose.

☐ 7. Battle's sign.

☐ 8. Bilateral orbital ecchymosis (Raccoon Eyes)

☐ 9. Unexplained focal neurological signs.

☐ 10. Other ______________________________

If questions arise please consult your supervising physician, neurosurgical resident, neurology resident or Emergency Service Attending. If this physician concurs in the need for skull radiography, add his/her name below.

Requesting Physician ______________________
(Please print)

Consulting Physician ______________________
(Please print)

(Radiologists and Reviewing Physicians--Use Other Side)

Department of Radiology Report:

	1. Fracture	☐
	2. Pineal Shift	☐
POSITIVE	3. Focal Bone Abnormality	☐
	4. Intracranial Calcification	☐
	5. Other ____________________	☐
NEGATIVE		☐

Radiologist ______________________________

RECORD REVIEW:

1. Effect on treatment plan.

2. Other tests done as a result of skull radiography findings.

3. Patient benefit received.

4. Other

Mr. ROGERS. Thank you very much, Dr. Phillips, for a very helpful statement and very interesting statistics on research done. Thank you.

Our next panelist will be Dr. Priscilla W. Laws, who is the associate professor of physics at Dickinson College.

We welcome you and are pleased to receive your statement.

STATEMENT OF PRISCILLA W. LAWS, PH. D.

Dr. LAWS. I was asked to describe myself a little. I am a combination of a scientist and a consumer advocate. I received a doctorate in nuclear physics from Bryn Mawr College in 1966 and have been studying the aspects of uses and misuses of diagnostic X-rays since 1972.

In addition to conducting research on the effective radiation doses associated with various common radiographic procedures, I have written articles and guides for radiologic technologists and consumers on medical and dental X-rays. I have just completed a 4-year term on the Bureau of Radiological Health Radiation Advisory Committee.

On the question of over use of X-rays, I would say that although medical and dental X-rays are very important diagnostic tools, their uses contribute to rising medical costs and may be causing radiation damage to exposed populations and their offspring. My purpose today is to discuss the possible extent to which X-rays are overused or misused, the estimated risks and costs associated with diagnostic X-ray exposures, as well as some of the apparent reasons for excess X-ray exposure to the U.S. population.

As was mentioned earlier, diagnostic X-rays constitute the largest single source of radiation exposure to the U.S. population. Most physicians and dentists believe that the overall benefits of diagnostic X-ray examinations outweigh any risks associated with them and are cost effective. Nevertheless, an increasing number of people working in radiological protection feel that diagnostic X-rays are overused and misused.

Because the appropriate uses of diagnostic X-rays and that radiation exposures necessary to obtain acceptable images are matters of individual professional judgment on the part of physicians and dentists, it is impossible to quantify the amount of unnecessary radiation dose to the U.S. population. We know that X-rays have been used in the practice of defensive medicine, as placebos, and in routine examinations of asymptomatic patients. We know that X-ray examinations result in excess radiation doses or have to be repeated because of poor techniques and technologists errors. For example, the authors of a recent report published by the Environmental Protection Agency assert that as much as a 50-percent reduction in radiation dose from diagnosic X-ray examinations might be possible without loss of medical benefits. (1) [1]

As to the question of risks, I can only summarize some of the studies that have been done before. There are epidemiological studies which indicate that diagnostic X-rays of unborn children and of the abdominal area in adults may increase the leukemia incidence 2 to 30 years after exposure (2), and X-rays can damage the reproductive cells of potential parents, causing genetic diseases in future generations. (3)

---

[1] Numbers in parentheses, see list of references p. 20.

There is no direct evidence that diagnostic X-rays of other regions besides the trunk are harmful. In fact, it is difficult to establish an exact relationship between biological damage and dose for the low levels of radiation which characterize diagnostic X-rays. It is widely accepted in the field of radiological protection that in the absence of concrete evidence, it is most prudent to assume that ionizing radiation involves a health risk which is proportional to the absorbed X-ray dose. This is known as the liner hypothesis, and it assumes that any amount of radiation absorbed by an individual, no matter how small, involves some risk.

The cancer or leukemia producing potential of various diagnostic procedures can be estimated for common X-ray examinations conducted under typical conditions. Estimates of relative radiation risks are contained in my book "X-Rays: More Harm Than Good?" published by Rodale Press and with the publishers permission, appropriate sections of the text have been attached to this statement for the record. It should be noted that the relative cancer or leukemia risks vary tremendously from examination to examination. The highest risk examinations include mammography, the upper GI, the barium enema, and the thoracic spine, while the lowest risk examinations appear to be those of the teeth, chest and extremities.

TABLE I.—AVERAGE EFFECTIVE DOSES OF COMMON X-RAY EXAMINATIONS (SOMATIC DOSES)

A. High Dose Examinations (more than 125 mrad or mrem per average examination): Mammography (breast examination); Upper GI Series (barium swallow); Thoracic spine (middle or dorsal spine); Lower GI Series (barium enema, colon examination); Lumbosacral spine (lower spine); and Lumbar spine (lower back).

B. Medium Dose Examinations (25–125 mrad or mrem per average examination): Intravenous Pyelogram (IVP, exam of kidney, ureter, and bladder); Cervical spine (upper spine); Cholecystography (gallbladder examination); K.U.B. (kidney, ureter, or bladder examination); Skull; and Lumbo-pelvic (examination of pelvis and lower spine).

C. Low Dose Examinations (less than 25 mrad or mrem per average examination) Chest: Hip or upper femur (hip or upper thigh examination); Shoulder; Dental (whole mouth or bitewing examination); and Extremities (feet, hands, forearm, etc.).

In terms of costs we know that the number of X-ray examinations has been going up dramatically in the past 15 years. In 1964 an estimated 77 out of every 100 people visited X-ray facilities. By 1970 Americans were making an estimated 179 million visits to X-ray facilities each year at a rate of 90 visits per 100 people. (4) The X-rays cost approximately $3 billion and represent about 4 percent of the total national expenditure for health care in that year. (5)

Because of rising costs and frequency of X-ray examinations the total costs of diagnostic X-rays were expected to rise to $4.8 billion by 1975. (6) I estimate that the average family of four in the United States is paying more than $100 a year for medical and dental X-rays.

TABLE II.—ESTIMATED NUMBER AND COST OF DIAGNOSTIC EXAMINATIONS IN 1970 [1]

Examination type	Number of exams (millions)	Average cost per exam	National expenditure (millions)
I. Medical X-rays	142.0	$17.19	$2,440.0
II. Dental examinations:			
(1) Bitewing	27.2	6.85	186.5
(2) Bitewing and periapical	8.9	8.50	76.5
(3) Full mouth series	7.4	17.67	130.7
(4) Periapical	19.9	5.00	99.5
(5) Other (panoramic cephalometric, et cetera)	4.4	17.67	77.7
(6) Total dental	67.8		570.9
III. Total medical and dental	210.0		3,010.0

[1] Based on data from the U.S. Department of Health, Education, and Welfare environmental assessment report on performance standards for diagnostic X-ray systems and their major components (August 1974).

I think there are a number of factors that are contributing to the overuse of X-rays. One of the factors has to do with insurance programs. Since 1950, there has been a rapid growth in both private and Federal insurance programs. In 1950, third parties paid for 32 percent of the Nation's personal health care, but by 1974, this had increased to 65 percent of the total.(7) This expansion of insurance coverage has been accompanied by a rise in medical care costs notably greater than the rise in prices for other goods and services.

Although the increase in medical costs has been attributed to the introduction of more expensive technologies and the ever-increasing utilization of diagnostic tests and therapies, health insurance has been primarily responsible for the whole trend toward more extensive and expensive health care. In the mid-1960's the Federal medicare and medicaid programs were added to the already expanding private insurance companies.

There is little dispute about the fact that both medicaid and medicare encourage the overuse of diagnostic tests. Cities which have large retirement populations abound with new storefront clinics which perform diagnostic tests paid for by medicare. An elderly man walking out of a storefront clinic commented to a television interviewer that "you go in with an aching ear and get X-rays from head to toe." The fact that medicane enables doctors and clinics to indulge in expensive diagnostic tests and yet does not pay full costs leaves patients in a double bind.

Recently an older woman ~~who had~~ injured her shoulder in a fall wrote to me. She received a chest X-ray which showed a shadow on her lung. Her doctor then ordered "25 X-rays, an electrocardiogram, and several blood tests." He asked her to go into the hospital for more tests. She informed him that all she had was medicare and asked him who was going to pay for the tests. He said, "Don't worry about it."

Her stay in the hospital lasted a week and involved 75 X-rays, brain scans, bone scans, two biopsies, a bronchoscopy, and several blood tests. Her doctor wanted to test her pancreas, and if he found nothing, he said he would open her chest.

I have a quote from her. She said in her letter:

> When I heard that I got dressed real fast and told him I wanted to leave the hospital. His face got scarlet and he said, "OK, but your blood is bad and I wouldn't be surprised if you have the same thing as Martha Mitchell." That was three weeks ago. I now feel fine. I spoke to my former doctor, who is retired. He said that he saw the records and they don't show a thing. The bills for over $3,000 are still piling up. I'm moving at the end of the month and will file bankruptcy as I haven't the money to pay for them.

A 70-year-old woman who was subjected to numerous X-rays commented:

> If he took one, he took a hundred. I wouldn't be surprised to read in the New York Times that doctors were legally padding medicaid bills by giving unnecessary X-rays.

Some insurance companies are requiring dentists to submit post treatment X-rays as substantiation for claims even when these X-rays do not contribute to the patient's treatment.

We must find better ways to provide people with adequate and affordable medical care without increasing unnecessary medical visits, treatments, and cost X-ray examinations and other costly diagonstic evaluations.

Another area of overuse is the area of routine examinations. Dr. Reskin already talked about routine skull exams and pelvimetries. Routine examinations are those in which people without any complaints or symptoms of illness are advised to submit to diagnostic tests. These routine examinations involve regular medical and dental checkups as well as mass screening programs in which large segments of the population are encouraged to undergo testing to determine the source of potential health problems. Several types of common routine examinations involve the use of X-rays studies. These studies include the X-ray examinations associated with regular physical and dental examinations, free mobile unit chest X-ray screening for tuberculosis and other respiratory disases, X-rays required for employment or hospital admission, and mammographic screening for breast cancer.

Screening programs and regular checkups are usually conducted on the grounds that people with unsuspected illnesses can have them diagnosed and treated at an early stage and, indeed, some cases of unsuspected disease are uncovered. However, regular examinations cost money, divert resources from other health programs and, in the case of X-rays, involve some degree of risk. The key question about various screening programs is not whether any disease is diagnosed, but rather whether enough cases of diseases are uncovered and successfully treated to justify the costs and risks associated with the examination.

Programs involving routine diagnostic tests are often introduced before the benefits, costs and risks are properly weighed against each other. An example is the recently discontinued mammographic screening program for breast cancer set up by the American Cancer Society and the National Cancer Institute.

One area of routine examinations, I think, that has varied widely is dental exams. Although the potential radiation risks associated with dental X-ray are extremely small, the routine use of dental X-rays is of questionable benefit and contributes greatly to spiraling cost of dental care.

My former dentist required routine X-ray examinations of all his patients every 6 months. He used to have his hygienist take several bitewing films before he even examined my mouth. This type of routine examination is practiced by many dentists.

It is difficult, if not impossible, to figure out what guidelines dentists are following in developing their procedures. And there seem to be no uniform standards by which dentists determine how often X-rays are really necessary. The American Dental Association recommends that:

> The dentist's professional judgment should determine the frequency and extent of each radiographic examination. Determination of the number of film exposures involved in a radiographic examination should be justifiable in terms of the expected yield of diagnostic information. (8)

In the absence of clear guidelines, it appears that many dentists in the New York area are opting for X-ray examinations as an integral part of routine checkups. A telephone survey of 500 dentists yielded the following statistics about the practices of dentists in the New York City area: Eighty-nine percent of the dentists ordinarily include a full set of X-rays [whole mouth] in the patient's first visit. Forty-one percent of the dentists repeat X-rays of at least part of the mouth during routine reexaminations every 6 months, and another 46 percent repeat them every year. (9)

The actual practices of dentists vary a great deal, but it is also clear from a number of letters I received from all parts of the United States that the practice of taking periodic X-rays is distressingly common. I noted with some surprise that each dentist has a different time period between examinations, and different numbers of films are exposed.

Another routine examination in the hospital that is overused, I believe, is the hospital chest X-ray exam. It is common practice for hospitals to require chest X-rays of all outpatients visiting their X-ray departments, regardless of what other X-ray studies that have been ordered. In addition, hospital inpatients are usually required to have chest X-rays before they can be admitted.

Hospital X-ray departments perform more chest examinations than any other type. Although 37 million chest X-ray examinations were being performed annually in hospitals by 1979, (10) there is no firm information about how many of these were conducted on a routine basis. However, the results of a series of hospital interviews conducted by the New York Public Interest Research Group indicate that the number is enormous. (11) Of the eight hospital administrators queried in the New York City Borough of Queens, four have preadmission procedures which normally include a chest X-ray for patients who enter the hospital. Another three hospitals do not include chest X-rays as part of their normal preadmission procedures, but interviewers were informed that doctors normally prescribe chest X-rays for their entering patients anyway.

Patients who are scheduled for surgery usually require a chest X-ray in order to be sure they can safely receive general anesthesia. However, this is no excuse for routinely X-raying every patient who enters the hospital. Most hospitals that automatically X-ray incoming patients claim to be screening primarily for tuberculosis, which is a highly communicable disease that could spread to other patients. However, this does not seem logical in terms of what is now known about tuberculosis and its detection.

The incidence of tuberculosis is currently at a low ebb in most areas in the United States, although the disease is still relatively widespread among people living in overcrowded, poverty level surroundings. Dr. John DeHoff, health commissioner for the city of Baltimore, commented in a 1976 newspaper interview that:

> If you have someone with no signs of lung trouble on physical examination and with no complaints about their chest, it's been shown in the medical literature that chest X-rays do no good.

Thus, even though the city of Baltimore has the highest per capita incidence of tuberculosis in the United States, the health department there does not advise the use of routine chest X-rays. Instead, they recommend a simple tuberculin skin test.

In the case of preemployment X-rays, we found that X-ray examinations are often conducted for the legal protection of employers. The most common of these examinations consists of the routine preemployment lower back X-ray series for workers doing heavy lifting. Some employers assume that an X-ray examination of the lower back can predict the chances of an employee developing a job related back disability. But some investigators have found evidence that this is not true. (12)

Although a recent conference on preemployment physical examinations (13) concluded that routine X-rays of the lower back might be valuable in assessing the degree of already existing disabilities, clear evidence supporting this contention was not yet available. Unfortunately, lower back or lumbar spine X-rays involve higher exposures than most other commonly used diagnostic examinations.

Another common preemployment examination is the chest X-ray required by certain States for job categories like nursing, teaching, and food handling.

Another example of the misuse of X-ray examinations for employees is the executive physical examination. Routinely prescribed by the management of some companies for top executives, the executive physical may subject asymptomatic individuals to X-ray examination of the spine, kidney, and upper and lower gastrointestinal tracts. The GI series and lower spinal examinations are among the highest risk examinations of all. In addition, the reproductive organs and a lot of red bone marrow, which is susceptible to leukemia, are in the primary X-ray beam in the lower trunk area.

X-ray examinations used routinely during pregnancy is another problem. The practice of exposing pregnant women to diagnostic X-rays which place the fetus in the direct X-ray beam is known to be potentially hazardous to the unborn child. (14) A developing fetus or embryo is much more sensitive to radiation damage than an adult receiving the same radiation dose. A study conducted by personnel at the University of California Medical Center concluded that there are harmful effects of X-rays to an unborn child at any stage of pregnancy. (15) Early in pregnancy, the risk of accidental miscarriage, congenital malformations, and brain damage predominate. After the fourth month, the most serious risk is that the unborn child may develop leukemia sometime during early childhood.

If it is true that the potential for damage exists in proportion to radiation dose, then those X-ray studies which place an embryo in the main X-ray beam should be avoided if at all possible. Thus, an X-ray study of a mother's abdominal region or lower back should not be conducted unless it is vital to the immediate treatment of a serious condition in the mother or unborn child. (16)

It was reported that in 1970, 23 percent of the 3½ million pregnant women in the United States were exposed to medical X-rays. (17) Nine percent of these examinations placed the unborn child in the X-ray beam.

The New York Public Interest Research Group telephone survey indicated that women of childbearing age are not usually asked by either physicians or technicians if they might be pregnant. (18) Of these women in the survey under the age of 50 who had received abdominal X-rays, two-thirds reported that they had not been asked about pregnancy.

In 1970, an overwhelming 88 percent of the fetal exposure to X-rays occurred during the last 3 months of the mother's pregnancy. (19) Most of these abdominal examinations conducted just prior to childbirth were taken to determine the size of a woman's birth canal or the location of the baby. Such examinations, known as pelvimetry, are still being conducted by some physicians on a large number of their patients, despite increasing evidence of the extra danger X-rays pose to unborn children.

A study by a group at the Bureau of Radiological Health indicates that results of X-ray pelvimetry on an expectant mother very seldom changes the course of her treatment. (20) Although the group indicated that further study is needed, their results suggest that except in very unusual circumstances, pelvimentry may well be a useless examination. This is discouraging when one considers that pelvimetry now constitutes the greatest single source of X-ray exposure of the fetus.

Another type of X-ray overuse is probably the thorniest of all, and that is the use of defensive X-rays. Ordering diagnostic X-rays which may prove beneficial in the treatment of patients is certainly legitimate. Because of the current malpractice climate, physicians and dentists are ordering more diagnostic tests than ever as a protection against possible lawsuits. One of the most common forms of defensive medicine involves the practice of ordering unnecessary diagnostic X-ray examinations. It has been estimated that between 20 and 30 percent of all medical diagnostic X-rays are ordered primarily for defensive purposes. (21) A number of studies indicate that the greatest overuse of X-rays for defense purposes occurs in the hospital emergency rooms with patients having head injuries. (22, 23)

Even if the defensive X-ray procedures constitute only 20 percent of the total number conducted, consumers are paying a tremendous price for the medical profession's malpractice protection in terms of both unnecessary health risks and dollars. It has been estimated that medical and dental X-rays cost Americans $4.8 billion in 1975. If 20 percent of the X-rays are ordered for defensive reasons, then almost $1 billion per year is going for X-rays which are not medically justified. Since the total awards to patients for malpractice settlements amount to only about $100 million per year, patients are paying 10 times more for defensive X-rays than they are getting back in settlements from all types of malpractice suits. And in any event, only a small percentage of the $100 million is awarded in cases involving failure to order appropriate X-rays. Thus, it appears that health professionals may be ordering an unreasonable number of defensive X-rays.

I want to talk a little bit about CAT scanners, because the introduction of new equipment often stimulates an overuse of diagnostic techniques.

The new units for computerized axial tomography are rapidly replacing some of the more traditional X-ray examinations.

The benefits of CAT scanners for brain studies are widely accepted, and experts feel that the newly developed body scanners are contributing to the early detection of cancers and other diseases in internal organs. In spite of the many potential benefits, radiologists admit that the ultimate value of body scanners cannot be assessed without more experience.

As hospitals and medical centers throughout the United States begin to install CAT scanners, voices of concern about the impact of their widespread use on medical costs have already been raised. Scanners cost from $350,000 to $600,000 each. Furthermore, this purchase price does not include the cost of constructing a lead-shielded room to house the machine, the training of technologists, or the yearly contract fee for maintenance. No comprehensive studies are available on the optimal number of CAT scanners needed in the United States. Nevertheless, some experts estimate that a ratio of one scanner for every 300,000 to 700,000 people should be adequate. (24, 25) But the interest in scanners has already led to needless and expensive duplication of them in places like Florida and Southern California where the ratio is about 1 per 75,000 individuals. (25)

The average cost to the patient of a CAT brain scan is currently more than $200, and experts estimate that a CAT scanner with a high rate of use can bring in $2,000 to $3,000 per day. There has been no apparent resistance from health insurance companies to footing the bills for scanning, but if costs rise, the insurers may raise objections.

Another problem is that scanning technology is developing very rapidly. With the first scanners barely 3 years old, manufacturers are already producing test models of third-generation scanners which will be faster, easier to operate, and cheaper to manufacture. This means that a $500,000 investment could very quickly become obsolete.

There will be pressure on health facilities which do purchase scanners to earn enough revenue to return their investments as quickly as possible. As more hospitals purchase scanners, economic pressures may induce them to perform scans on more and more patients who don't really need them. This is likely to result in additional increases in medical costs and more unnecessary radiation exposure to patients.

I want to just very quickly summarize some of the reasons for excess dose. One, of course, is lack of gonad shielding. Men, women, and children who are potential parents run some risk of passing defective genes to their offspring if their reproductive organs or gonads are exposed to X-rays. If an examination places the reproductive organs in the X-ray beam, lead shielding should be placed in front of them, provided that the shielding does not interfere with the examination. This is easily accomplished in men and boys by covering their testes with lead shields which absorb X-rays. Unfortunately. The female ovaries are more difficult to protect. It is estimated that the conscientious use of gonadal shields for males would result in a 75-percent reduction in the testicular dose to the male population (26) and that, of course, would mean that correspondingly less genetic risk to future generations.

The improper collimation. Although patients are seldom aware of improper X-ray beam restriction, it, too, is a major factor in the unnecessary exposure of patients to radiation. Over half of all medical X-ray examinations expose patients to additional radiation because the beam area is larger than the size of the film. And 15 percent of all X-rays appear to have a beam area which is more than two times larger than the film area. (27) The new devices for beam restriction that have been mandated by recent law have probably started cutting down on this some.

POOR IMAGES AND IMPROPER POSITIONING

Several studies have shown that the primary reason X-rays are repeated is that the image on the film is too dark or too light, while the second most common cause of retakes is improper positioning of the patient. (28) Films which are too dark or too light usually result either from failure to choose the proper exposure settings on the X-ray machine or from improper development of the film.

Exams which must be repeated due to technologist errors or other technical failures are an obvious source of unnecessary radiation exposure and wasted expense. However, these repeated examinations may only represent the tip of the iceberg, since there is evidence that many of the X-rays which are considered to be of "acceptable quality" by technologists (and even by some physicians) are so poor that they contain no useful diagnostic information. Dr. Benjamin Felson, a leading expert in chest radiology, stated in 1975 that about half the chest films used in mining communities to diagnose black lung disease were of unreadable quality. (29) Patients are seldom aware of this source of misdiagnosis as well as unnecessary radiation exposure and expense.

SUBOPTIMAL EXPOSURE SETTINGS

In some instances, a combination of exposure settings is used to produce a film which is diagnostically acceptable to the radiologist but causes more radiation to be absorbed by the patient than necessary. In such a case there may be an alternate set of exposure factors which exposes patients to less radiation and results in an even better quality X-ray film. Technologists should take the extra time to figure out the combination of exposure settings that will expose the patient to less radiation while still producing a high quality X-ray film.

I want to come, finally, then to some very broad suggestions for how to reduce unnecessary risks and costs from diagnostic X-rays.

Mr. ROGERS. Excuse me. I wonder if we can interrupt at this point. There is a call to the floor for a vote, and Members must respond. Therefore, we will stand in recess for 10 minutes, and then we will continue with your testimony.

Thank you.

[Brief recess.]

Mr. ROGERS. The subcommittee will come to order please.

We interrupted Dr. Laws' testimony. You may proceed.

Dr. LAWS. I was just going to remind the committee that exposure to unnecessary diagnostic X-rays can increase the incidence of cancer, leukemia, and genetic diseases in the general population without offsetting benefits.

Furthermore, the conduct of unnecessary examinations can raise health care costs and divert resources in the healing arts from more productive activities. Thus, it is important to consider additional ways that the Federal Government can reduce the incidence of unnecessary diagnostic X-ray doses and examinations without diminishing the quality of medical care.

An interagency working group consisting of representatives of the Department of Health, Education, and Welfare and the Environmental Protection Agency has recently developed and is aimed at reducing unnecessary X-ray exposure in Federal health care facilities. (30)

These recommendations were approved by President Carter in January of this year. I would like to see similar Federal guidelines and regulations developed that can be applied to all X-ray facilities.

The Bureau of Radiological Health has made substantial progress toward this end by initiating programs designed to yield recommendations which cover a range of critical X-ray protection issues.

There is more to do in this area and I would underscore, Mr. Chairman, the vital role that you and the subcommittee play and protection efforts continue to be supported and that new initiatives are taken to minimize the radiation risks placed upon patients and the costs associated with the diagnostic X-ray examinations.

I have divided my recommendations into general recommendations, recommendations that might reduce the number of examinations and, finally, recommendations that might reduce the dose of examinations considered necessary.

The first recommendation is that we use the best information currently available about organ radio sensitivities and doses to assess the magnitude of various risks associated with common diagnostic X-ray procedures.

The second recommendation is that we continue efforts to improve the curricula on good X-ray practice and the bioeffects of low-level radiation in medical and dental schools as well as in the training programs for all personnel using diagnostic X-rays.

The third recommendation is that we continue efforts to inform consumers about good X-ray practices and the benefits and risks of X-ray procedures.

As to the second set of recommendations to reduce number of examinations, my fourth recommendation is that we study the cost effectiveness and risk-benefit factors for all diagnostic examinations used for hospital chest examinations, employment chest examinations, employment lower spine examinations. mammography, executive physicals involving diagnostic X-rays, dental examinations, pelvimetric examinations, and periodic physical examinations involving diagnostic X-rays.

The fifth recommendation is that we prohibit the use of routine screening that cannot, according to current understanding be shown to be both cost effective and more beneficial than potentially harmful. A preliminary analysis of benefit cost and cost effectiveness for some of these examinations is contained in a 1977 National Academy of Science study conducted for the Environmental Protection Agency. (31)

The sixth recommendation requires that X-ray personnel ask all premenopausal females scheduled for abdominal procedures if they might be pregnant and that postponement be considered for female patients who are or suspect they might be pregnant.

Recommendation 7: We should study ways to modify private and Federal insurance programs so that the use of diagnostic tests and post-treatment examinations is minimized without significant reduction in the quality of patient care.

Recommendation 8: We should initiate a study of the factors which influence the use of defensive X-rays, and make recommendations about measures which might reduce the incidence of defense X-ray examinations which have little potential medical benefit.

Recommendation 9: Regulations should be developed to prevent the overproliferation of sophisticated X-ray units operated in a given region in order to minimize the overuse of procedures which require complex and expensive equipment, such as CAT scanners.

The third set of recommendations are to reduce patient dose from examinations.

Recommendation 10: Continue in the development of equipment performance standards as new diagnostic X-ray devices become available. Standards for CAT scanners, for example, are under development at the Bureau of Radiological Health.

Recommendation 11: Develop regulations or guidelines on the use of technique factors, such as entrance skin exposure, KVP and HVL gonadal shields, appropriate to the equipment and materials in use to maintain minimum practical effective doses compatible with the desired image quality.

And the final recommendation, development of standards for either licensure or credentialing for all types of X-ray machine operators which include training in both techniques and current background information on the biological effects of low-level radiation.

Thank you.

[Testimony resumes on p. 54.]

[Attachments to Dr. Laws' prepared statement follows:]

REFERENCES

1. U.S. Environmental Protection Agency (ORP/CSD) Publication 72-1, ESTIMATES OF IONIZING RADIATION DOSES IN THE UNITED STATES 1960-2000, prepared by A. W. Klement, Jr. et al. (Washington, D.C.: Environmental Protection Agency, August 1972), p.98.

2. A. M. Stewart and G. W. Kneale, "Radiation Dose Effects in Relation to Obstetric X Rays and Childhood Cancers," LANCET 1 (1970): 1185-88; R. Gibson et al., "Introduction in the Epidemiology of Leukemia Among Adults," Journal of the National Cancer Institute 48 (1972): 301-311.

3. International Commission on Radiological Protection, The Evaluation of Risks From Radiation, Publication no. 8 (New York: ICRP, 1966), p. 40.

4. U.S., Department of Health, Education, and Welfare (FDA) Publication 73-8047, Population Exposure to X Rays U.S. 1970 (Rockville, Md.: Public Health Service, November 1973), p. 27

5. U.S., Department of Health, Education, and Welfare (Code of Federal Regulations) Publication, Environmental Assessment Report: Performance Standard for Diagnostic X-ray Systems and Their Major Components, 21 CFR 1020.30-1020-32; and Related Interpretive Policy Concerning the Assembly and Reassembly of Diagnostic X-ray Components, 21 CFR 1000.16 (Rockville, Md.: Public Health Service, September 1976), Appendix B, pp. 1-4.

6. Ibid.

7. U.S. Department of Health, Education and Welfare (SSA) Publication 75-11909, Medical Care Expenditures, Prices and Costs: Background Book (Washington, D.C.: Department of Health, Education, and Welfare, 1975), p. 14.

8. Journal of the American Dental Association 90 (January 1975): p.171.

9. Deborah VanBrunt, Consumer Perspectives on X Rays (New York: New York Public Interest Research Group, 15 November 1976).

10. U.S., Department of Health, Education, and Welfare (FDA) Publication 73-8074, Population Exposure to X Rays U.S. 1970 (Rockville, Md.: Public Health Service, November 1973).

11. "Consumer Perspectives on X Rays".

12. Henry LaRocca et al., "Value of Pre-employment Radiographic Asseessment of the Lumbar Spine," Industrial Medicine and Survery 39 (June 1970); 253-58; J. T. Redfield, "The Low Back X Ray as a Pre-employment Screen Tool in the Forest Products Industry," Journal of Occupational Medicine 13 (May 1971): 219-26; American College of Radiology, Conference on Low Back X Rays in Pre-employment Physical Examinations, summary report and proceedings (Tuscon, Ariz.; January 1973); 164-44.

13. Ibid., p. 198

14. U.S., Public Health Service (FDA), "X-ray Effects on the Embryo and Fetus: A Review of Experimental Findings," prepared for the Bureau of Radiological Health by Robert Rugh and William Leach (Rockville, Md.: September 1973); U.S., Radiological Health Sciences Education Project Publication no. 874, "A Concept and Proposal Concerning the Radiation Exposure of Women," prepared under contract no. FDA 72-13 with the Bureau of Radiological Health (FDA), by Reynold F. Brown et al. (Rockville, Md.: Bureau of Radiological Health); A. M. Stewart and G. W. Keale, "Radiation Dose Effects in Relation to Obstetric X Rays and Childhood Cancers," *Lancet* 1 (1970): 1185-88; Irwin D. J. Bross and Nachimuthu Natarajan, "Leukemia from Low Level Radiation: Identification of Susceptible Children." *New England Journal of Medicine* 287, no. 3 (20 July 1972): 107-10.

15. "A Concept and Proposal," p. 9.

16. U.S. Department of Health, Education, and Welfare, *X-ray Examinations - A Guide to Good Practice* (Rockville, Md.: *Bureau of Radiological Health (1970)*, p. 6

17. U.S. Department of Health, Education, and Welfare (FDA) Publication 75-8029, "Considerations of Possible Pregnancy in the Use of Diagnostic X Rays," Health Physics in the Healing Arts, Seventh Midyear Topic Symposium, Health Physics Society, December 1972, p. 599.

18. *Consumer Perspectives*.

19. U.S. Department of Health,Education and Welfare, Public Health Service Publication no. 1000, series 22, no. 5, *Medical X-ray Visits and Examinations During Pregnancy U.S., 1963*, prepared by Morton L. Brown and Arne Nelson (Washington, D.C.: Department of Health, Education, and Welfare, June 1968), p. 7.

20. Kevin Kelly et al., "The Utilization and Efficiency of Pelvimetry," *American Journal of Roentgenology* 125, no. 1 (September 1975): 66-74.

21. D. H. Twire and E. J. Potchen. *A Dynamic Systems Analysis of Defensive Medicine* (M.S. Thesis, MIT, June 1973), and *Duke Law J.*, 939 (1971)

22. Robert Brook et al., "Effectiveness of Non-Emergency Care via the Emergency Room" *Annals of Internal Medicine* 78 (1973) and R. S. Bell and J. W. Loop, "The Utility and Futility of Radiographic Skull Examinations for Trauma," *New England Journal of Medicine* 284 (4 February 1971): 236-39.

23. F. Roberts and C. Shopfner, "Plain Skull Roentgenograms in Children with Head Trauma," *American Journal of Roentgenology* 114 (1972): 230-34. Nash D. Harwood et al., "The Significance of Skull Fractures in Children. A Study of 1, 187 Patients," *Radiology* 101 (1971): 151-55.

24. Massachusetts Department of Public Health, Report on CT Scanning (24 February 1976, attachment IVk).

25. Quotation from Jonathan Spivak, "A'Glamor Machine' Is Hailed by Doctors as a Boon to Diagnosis," Wall Street Journal 186, no. 114 (10 December 1975).

26. U.S. Department of Health, Education, and Welfare (FDA) Publication 74-8028, Gonadal Shielding in Diagnostic Radiology (Rockville, Md.: Bureau of Radiological Health, June 1974), p. 3

27. U.S., Department of Health, Education, and Welfare (FDA) Publication 73-8047, Population Exposure to X Rays U.S. 1970 (Rockville, Md.: Public Health Service, November 1973), p. 94.

28. U.S., Department of Health, Education, and Welfare (FDA) Publication 76-8016, A Study of Retakes in Radiology Departments of Two Large Hospitals, prepared by Bruce H. Burnett et al. (Rockville, Md.: Department of Health, Education, and Welfare, July 1975), and the references cited therein.

29. Interview of Benjamin Felson, M.D., Medical World News, February 1975.

30. U.S., Environmental Protection Agency Publication 520 14-76-019. Radiation Protection Gudiance for Diagnostic X-rays (Washington, D.C.: Environmental Protection Agency, Oct. 1976).

31. U.S., Environmental Protection Agency Publication 520 4-77-003. Considerations of Health Benefit - Cost Analysis for Activities Involving Ionizing Radiation Exposure and Alternatives, BEIR II Report. (Washington, D.C.: Environmental Protection Agency, 1977).

CHAPTER 12
HOW X RAYS AFFECT PEOPLE

Determining Effects on People

The potential for danger from x rays and other forms of radiation has often gone unnoticed in the past because the damaging radiation cannot be seen or felt. Except for situations in which people are exposed to enormous amounts of radiation, signs of damage are not noticeable until some time after exposure, perhaps a number of years.

Three units are commonly used in discussions of the potential biological effects of x rays and other types of radiation: the roentgen, the rad, and the rem. The roentgen is an approximate measure of the radiant energy to which a person or object is exposed, while the rad and rem provide a measure of the amount of energy actually absorbed by an exposed object.

Although on a technical level each unit is defined differently, for the purpose of the general discussion in this book, these units can be used interchangeably. One roentgen, rad, or rem represents a fairly large amount of radiation when compared to the average natural background dose received annually. For example, the average whole-body radiation dose received from natural sources (background radiation) in the United States is about 0.084 rems per year.[1] Often millirad (mrad), millirem (mrem), or milliroentgen (mr) are used instead. The prefix milli means 1/1000, so that 1 rem = 1000 mrem. Expressed in terms of the smaller units, the average whole-body dose in the U.S. due to background radiation is 84 millirems per year. (See Appendix A for a more detailed discussion of these units.)

It is estimated that the average resident of the United States receives an abdominal dose of 73 mrem per year,[2] primarily from medical x rays. Thus, the average abdominal dose received from diagnostic x rays is just slightly less than the abdominal dose received from natural background radiation in the United States.

Effects of Moderate and High Doses of Radiation

Experiments with animals and observations of people exposed to much larger doses of radiation than those associated with diagnostic x rays have provided valuable information about effects of radiation on living organisms.[3] The known effects are of two kinds. One set of effects directly influences the health of the exposed individual. These effects are known as *somatic effects.* Another set of effects which influence the health of the off-spring of the exposed individual are known as *genetic effects,* and are produced only when the reproductive organs (ovaries and testes) are exposed to radiation.

Somatic Effects

A study of American radiologists exposed to medical x rays in their occupations and two control groups consisting of other physicians indicated that on the average, radiologists in the United States have a higher incidence of cancer than their medical co-workers.[4]

The tragic exposure of a large number of Japanese people to the very high levels of radiation from the atomic bomb blasts in Hiroshima and Nagasaki in 1945 has added greatly to our understanding of the harmful effects of radiation.[5] When very high doses of radiation are absorbed rapidly (when more than 50 rems are received at a rate faster than 1 rem per minute), like those received by some Hiroshima victims, radiation sickness and in some cases death occurs within a few days or weeks after exposure. Other Hiroshima survivors who received somewhat less radiation and lived for a period of years after the atomic explosion had significantly more cataracts, cancers, and leukemia than an equivalent unexposed population. Pregnant women who received large doses of radiation and who survived the holocaust bore children who had an abnormal number of birth defects and a greater chance of developing cancer or leukemia. The number of miscarriages and stillbirths for this group of pregnant women was also significantly greater than average. Young children exposed to radiation suffered from many more health problems in subsequent years than adults receiving the same doses, although it was found that survivors of all ages who absorbed radiation had a greater risk of developing cancer or leukemia, or giving birth to deformed children in later years.

These studies of atomic bomb survivors indicate that when large amounts of radiation are absorbed rapidly by an individual, the risk of subsequently developing cancer seems to be directly proportional to the radiation dose received. Thus a victim who absorbs twice as much radiation runs twice the risk of developing cancer in later years. This same type of proportional relationship between high radiation doses and chances for developing leukemia and certain other long term somatic effects has also been established for animals tested in laboratories, and for children who were exposed to diagnostic radiation before they were born,[6] as well as for British patients who received large doses of x rays while being treated for a spinal disease known as ankylosing spondylitis.[7]

Genetic Effects

There is no entirely convincing data available on the ways in which radiation actually damages the genes and reproductive organs of humans. For the most part, we know these organs must be damaged by observing the higher rates of genetic illnesses present in the children of people whose reproductive organs have been exposed to high levels of radiation. However, a tremendous number of experiments have been performed on laboratory animals (such as mice and fruit flies) exposed to known amounts of radiation, and scientists believe the results of these experiments are indicative of the kinds of genetic damage incurred by humans. There is evidence that the reproductive material in human cells is somewhat more susceptible to damage than that in the cells of mice.[8] Thus, it is believed that radiation of the reproductive organs of humans can cause offspring to have a higher rate of mental retardation, cancer, ill health, and birth abnormalities. Except at very high doses, the amount of genetic damage done by radiation appears to be proportional to its dose and unrelated to the rate at which the reproductive organs are exposed. Harmful effects on the reproductive material (chromosomes) in human cells have also been observed directly when the cells are exposed to x rays or other forms of ionizing radiation.[9]

It is felt that laboratory data obtained from irradiating mice provides the most significant information about the possible genetic effects of radiation on humans.

The Effects of Radiation on Living Cells

Cells are the building blocks of living organisms. Some scientists believe that both the genetic and somatic damage associated with radiation exposure can be traced to the way in which radiation affects living cells. In any healthy organism some cells are dying while others are reproducing, replenishing, or increasing in number. Cells which are exposed to radiation often die or lose their ability to reproduce properly. Radiation loses its energy in passing through a cell by breaking apart some of the complex chemical bonds in the cell. As a consequence, the chemical bonds characterizing the structure of the genes in the cell nucleus, which directs its reproduction, can be altered either directly or indirectly by the radiation.

The ability of cells to reproduce accurately is quite important, and it is very probable that the impairment of the reproductive ability of cells in the human body results in increased susceptibility to cancer and other diseases. The process of aging is also believed to be related to the reproductive ability of cells in an organism.

When a sperm or egg cell from the human reproductive system is exposed to ionizing radiation, the arrangement of the basic genetic material, which contains instructions for the construction of offspring, may be altered or destroyed. These rearrangements, which are called mutations, may result in the failure of the cell to contribute to the reproductive process. A more serious consequence, however, is that such a damaged egg or sperm cell may produce offspring with physical, mental, or genetic damage. A number of illnesses and birth defects have now been attributed to genetic damage or mutations of one type or another.

It is well established that in humans the potential for harm from radiation exposure is greater for growing individuals whose cells must undergo rapid division to support growth. The embryonic stage is the most sensitive of all to radiation damage. However, in both adults and children some organs and tissues discard and replenish cells more rapidly than others. Organs and tissues which are more sensitive to radiation exposure than others include the thyroid and the red bone marrow where blood cells are manufactured.

Effects of Low Doses of Radiation

The effects on humans of low doses of radiation (less than 25 rem) similar to those delivered during common diagnostic x-ray examinations are not immediately noticeable. Indeed, since the discovery of x rays in 1895, there has been an ever-increasing awareness of some of the more subtle long term health effects of radiation. This fact is rather graphically illustrated by the way in which permissible doses for individuals working in the presence of radiation have declined over the years (see Fig. 1). Since 1940 the permissible whole-body occupational dose has decreased five-fold. Currently, it is believed that a person who is exposed to x rays during a medical or dental examination may have a

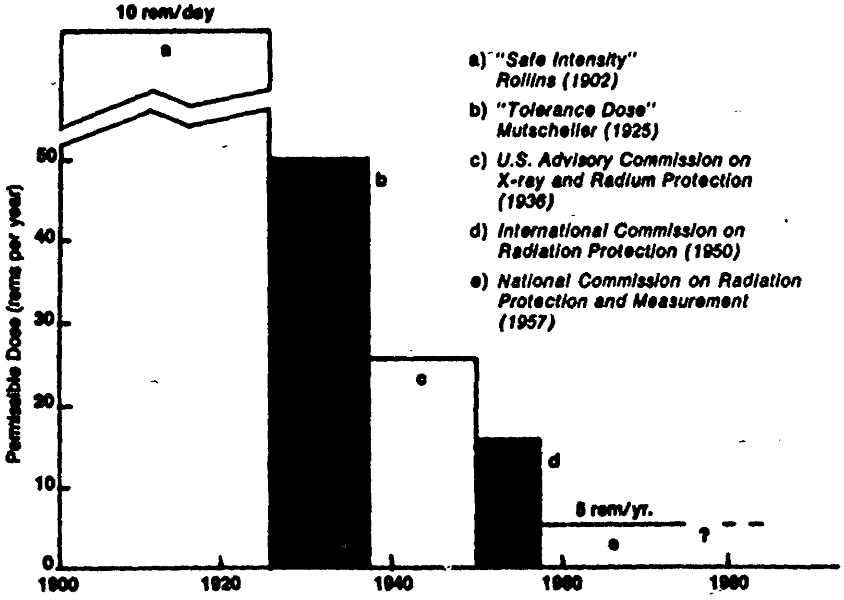


Fig. 1 — Historical trend in permissible whole body occupational dose

slightly greater chance of developing cancer or leukemia in later years. However, even if one of these illnesses develops, it would be impossible to trace its cause back to an x-ray examination. This is due to the fact that individuals are also exposed to other cancer-causing agents such as air pollution, drugs, and natural radiation.

As we noted earlier, at moderately high doses (25 to 50 rem) and dose rates a statistical relationship between radiation exposure and various cancers and leukemias has been observed in both humans and laboratory animals. For low doses, however, it is more difficult to separate the effects of radiation on humans or laboratory animals from other influences in the human or laboratory environment. When conducting experiments on the effects of very low doses of radiation on mammals, scientists need to study a very large group of animals in order to obtain valid results. This makes direct observations on humans quite difficult.

Until recently there was not much evidence that exposure to diagnostic x rays affected human health. One recent study has shown, however, that exposure to diagnostic x rays increases the chances of unborn children developing cancer or leukemia during childhood.[10] Although this study indicates that the probability of developing one of these conditions is in proportion to the radiation dose delivered to the fetus, these results are not conclusive, since it is easy to argue that the relatively poor health of those mothers who had x-ray examinations during pregnancy caused the increased susceptibility of their offspring to childhood cancers. A more recent study, supported by the National Cancer Institute, identifies certain types of children as more susceptible to radiation damage than others. In particular, the study indicates that children with a history of allergies or certain bacterial diseases were up to ten times more likely than other children to develop leukemia after being exposed to diagnostic x rays before birth.[11]

In 1972 a study *linking leukemia with the exposure of adults to diagnostic x rays* was published.[12] In this study the development of excess cases of leukemia in adult males was traced to previous diagnostic x-ray examinations. For some unknown reason the females in the study group did not show a significant increase in leukemia.

Many more sophisticated studies will be necessary before the full story of how diagnostic x rays are affecting humans is unraveled. At present we can only make judicious estimates of how low level x-ray doses affect humans, on the basis of other evidence.

In the laboratory there are quite strong indications that the response of mice to radiation dose is similar to the response of humans.[13] Both genetic and somatic radiation damage to laboratory mice and their reproductive cells have been observed at relatively low doses.

The Linear Hypothesis

Since it is difficult to establish an exact relationship between biological damage and dose for low levels of radiation, many scientists believe that in the absence of concrete evidence it is most prudent to assume that ionizing radiation involves a health risk to the exposed individual in proportion to the dose absorbed by that individual. This is known as the linear and non-threshold hypothesis. This hypothesis assumes there is no threshold below which radiation is harmless. Thus, *under the linear non-threshold hypothesis any amount of radiation absorbed by an individual, no matter how small, involves some risk to the health of that individual and/or his or her potential offspring.*

There is evidence, however, that indicates that certain effects induced by high radiation doses are not caused by lower doses.[14] For example, many Hiroshima victims who absorbed large doses of radiation in their eyes developed cloudy films or cataracts over the eye lenses in later years. Cataracts were also induced in the eyes of laboratory animals exposed to large doses. On the other hand, animals exposed to lower

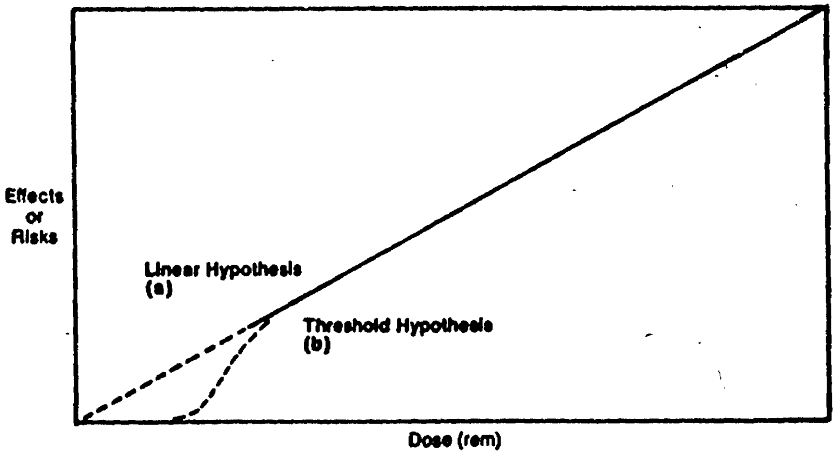


Fig. 2 — Relationship between radiation dose and effect using (a) the Linear Hypothesis, and (b) a Threshold Hypothesis

doses of radiation did not develop any cataracts. Cataract induction appears to be a threshold effect in the sense that there seems to be a dose below which radiation does no detectable damage to the lens of the eye. However, many scientists believe that genetic damage can be caused at even the lowest levels of radiation, that there is no threshold for this type of damage.[15] Since the question of whether or not a threshold exists for radiation damage is a matter of controversy, it is interesting to speculate about the problem in terms of the effects of radiation on the cells which make up the human body.

When ionizing radiation, like an x ray, passes through a cell, the cell may be damaged. This damage can either destroy the cell, impair its ability to reproduce, or cause it to reproduce with incorrect genetic information. The effect of high levels of radiation on an organism is serious because many of its cells are damaged and destroyed. At lower doses fewer cells are damaged. In either case, the number of damaged cells is roughly proportional to the amount of radiant energy (or dose) absorbed, no matter how small it is.

If individual cells have mechanisms for repairing radiation damage, then there may be a threshold dose below which radiation causes no permanent damage. However, the 1972 study linking leukemia in adult males to diagnostic x-ray doses suggests that if a threshold dose exists for adult males, it must be less than the doses delivered during some of the common diagnostic x-ray examinations.

In this book, I have assumed that the linear hypothesis is a reasonable working hypothesis for protection purposes. This assumption has also been made by official advisory groups including the International Commission of Radiological Protection (ICRP) and the National Council on Radiation Protection and Measurement (NCRP) in originally establishing the guidelines used for the protection of people working near radiation sources. In addition, scientists representing the prestigious National Academy of Sciences (NAS) gave strong support to the linear hypothesis in its recently published study (known as the BEIR Report) on the effects of low level ionizing radiation.[16]

The American College of Radiology has also taken the position that ". . . the prudent course at the present time is to assume that (radiation) effects may be initiated in a single cell and to assume that there is no lower limit to the radiation dose which might be considered injurious." [17]

CHAPTER 13
RISKS ASSOCIATED WITH X-RAY DIAGNOSIS

The radiation risks associated with an annual exposure to diagnostic x rays span a wide range, from examinations which may be comparable to regular cigarette smoking during a given year, to those which involve negligible risks. Pregnant women, young children, and potential parents are usually subjected to more risks in a given examination than other people. There are additional risks associated with certain diagnostic examinations involving the use of a contrast medium. These risks are caused by the introduction of the medium into the body and not by the x rays.

In general, examinations of organs and tissues in the abdominal regions involve significantly more somatic and genetic exposure than other examinations for several reasons. First, the abdominal region is filled with relatively dense tissues, so more x rays must be used during these examinations. Second, a relatively large film is used, thus exposing a large area of the body to x rays. Third, the reproductive organs are in the abdominal region. Finally, special risks to the unborn child are involved when abdominal x rays are used on pregnant women.

How Risks are Expressed

In addition to radiation exposure, many other typical human activities such as taking drugs, riding in a car, or smoking entail risks. These kinds of risks are classified as somatic, meaning that they are potentially harmful to individuals. Exposure of potential parents to radiation and certain drugs involves genetic risks, which only affect individuals in future generations. Taking both somatic and genetic risks into account when considering diagnostic x rays makes estimation of the risks and benefits more complicated.

Until recently, very little attention was given to obtaining numerical estimates of the risks or potential for harm associated with familiar activities. Even in cases where numbers have been assigned to risks, relatively few people use such information and change their habits or conduct accordingly. A recent exception to this is in the case of cigarette smoking; the link between smoking and lung cancer deaths and other health conditions has motivated many individuals to quit smoking. If we are to begin taking more responsibility for our own health care, we must become concerned about the risks involved in various forms of medical diagnosis and treatment.

Several approaches describe the risks associated with various activities. Some analysts have attempted to devise a suffering scale for health problems that may result from certain activities. For example, using such a scale, a fatal radiation-induced leukemia would be much higher on the suffering scale than a skin cancer which may be painful but which is rarely fatal. Another way to express risk is to place an economic value on induced disabilities or deaths. Such an economic analysis would add medical expenses to the loss of an average individual's income from employment.

The easiest method to use in relating radiation dose to risk is to estimate the number of excess deaths that would be expected if a specified number of people were all exposed to the same hazard. This method has been used to link the probability of developing lung cancer to smoking cigarettes. For example, according to a study conducted by Doctors Hammond and Horn, about 130 additional people out of one million regular pack-a-day smokers will probably die of lung cancer each year.[1]

Risk estimates for various x-ray diagnoses, like that for smoking, must be approximate. Scientists do not know enough about the precise relationship between absorbed dose and risks. Even if they did, the absorbed dose received from specific diagnoses depends on the techniques and equipment used to conduct each individual examination. For this reason, a reasonable way to express the risks involved in each type of x-ray examination is to calculate the risks using good equipment and techniques and those using poor equipment and techniques. We can then assume that the average risk falls somewhere between these two extremes.

What Are the Risks of Diagnostic X rays to Your Health?

Estimating the risk of death from cancer or leukemia for various x-ray examinations is complicated by the fact that it depends on the age and susceptibility of the exposed individual. Also, each examination exposes different organs and tissues in the body to radiation. Areas of the body like the red bone marrow and the thyroid are much more sensitive to damage by radiation than muscle or skin. Recent scientific publications have described the relative likelihood that various critical organs will develop cancer after receiving a given radiation dose.[2] If we know the skin dose (amount of radiation absorbed by the skin), the voltage of the x-ray tube and type of filter used, as well as the organs in the main beam, we can use these figures to compute a cancer producing or "effective dose" for a given x-ray examination.[3]

"Effective doses" are listed in Table 1 (later in this chapter) and Appendix C for some common x-ray examinations conducted under average conditions. A recent report published by the National Academy of Sciences, known as the BEIR Report, estimates using the linear hypothesis (see Chapter 12) that a whole-body dose of one rad or rem received by a million individuals each year causes an average of 80 excess deaths from cancer annually.[1] If the "effective dose" concept is valid, then one rad of effective dose would affect the risk of cancer and leukemia in the same way as one rad of whole-body dose.

The average number of deaths per rad should be considered an upper limit, since it is still possible that discovery of a threshold dose in the future may indicate that some of the lower dose diagnostic x-ray examinations involve little or no risk.

The "effective doses" and thus the cancer risks from different types of x-ray examinations vary widely. As shown in Appendix C, a lower gastrointestinal, or GI, examination conducted under average conditions may involve as much cancer risk as smoking somewhere between five and 20 cigarettes every day for a year. On the other hand, average examinations of the extremities or dental examinations involve less risk than smoking even one cigarette per day. The cancer risk associated with the average U.S. background radiation dose of 84 millirems per year [5] is comparable to smoking about one cigarette a day. Thus, typical examinations span a wide range of maximum risk.

Thus, GI examinations, which deliver the highest "effective dose" of any of the common procedures, may involve risks of fatal cancer comparable to the fatal lung cancer risks associated with regular smoking. (See Tables 1, 2, and 3, later in this chapter, for details.) On the other hand, a hip or thigh examination is about five to 10 times less risky than a gastrointestinal examination, and the "effective dose" of about 100 millirems per year received from hip or thigh examinations is comparable to the average background radiation dose in the United States.

Risks to Future Generations

Genetic risks to potential parents from x rays are difficult to compare directly to the risks of smoking and other activities, but information from the BEIR Report indicates that when the reproductive organs are included in the main beam, risks to future generations are similar to those encountered in submitting to x-ray examinations which are in the high dose somatic category. Table 2 and Appendix C give data on the average male and female reproductive organ doses for various examinations.

Non-Radiation Risks

Some diagnostic x-ray procedures involve the introduction of a contrast medium into the body in order to highlight certain organs or arteries. Contrast films are now quite common, and most contrast studies involve little risk. However, several types of studies involve added risks associated with the introduction of the contrast "dye" into the body.[6] The dangers of contrast-medium examinations include the potential for inducing a stroke or causing nerve damage when the dye is being introduced into the body. Some of the higher risk contrast x-ray examinations are listed in Table 4.

Since contrast examinations make up such a small percentage of the total number of x-ray examinations, the overall risks to the population from diagnostic x rays are still due primarily to radiation effects.

TABLE 1: AVERAGE EFFECTIVE DOSES OF COMMON X-RAY EXAMINATIONS (SOMATIC DOSES)

A. High Dose Examinations (more than 125 mrad or mrem per average examination)

- Mammography (breast examination)
- Upper GI Series (barium swallow)
- Thoracic spine (middle or dorsal spine)
- Lower GI Series (barium enema, colon examination)
- Lumbosacral spine (lower spine)
- Lumbar spine (lower back)

B. Medium Dose Examinations (25-125 mrad or mrem per average examination)

- Intravenous Pyelogram (IVP, exam of kidney, ureter, and bladder)
- Cervical spine (upper spine)
- Cholecystography (gallbladder examination)
- K.U.B. (kidney, ureter, or bladder examination)
- Skull
- Lumbo-pelvic (examination of pelvis and lower spine)

C. Low Dose Examinations (less than 25 mrad or mrem per average examination)

- Chest
- Hip or upper femur (hip or upper thigh examination)
- Shoulder
- Dental (whole mouth or bitewing examination)
- Extremities (feet, hands, forearm, etc.)

See Appendices A, B, and C for more details.

TABLE 2: AVERAGE DOSE TO THE REPRODUCTIVE ORGANS FROM COMMON X-RAY EXAMINATIONS (GENETIC DOSES)

A. **High Dose Examinations** (exposure of male gonads, more than 200 mrad per average exam)

- Lower GI (barium enema, colon exam)
- Intravenous Pyelogram (IVP, exam of kidney and ureter)
- Lumbar spine (lower back)
- +Lumbo-pelvic (exam of pelvis and lower spine)
- +Hip or upper femur (exam of hip or thigh)

B. **Medium Dose Examinations** (exposure of male gonads between 10-200 mrads per average exam)

- Upper GI (barium swallow)
- *Cholecystography (gallbladder exam)
- Thoracic spine (middle spine)
- *Upper GI (barium swallow)
- Abdomen
- K.U.B. (kidney, ureter, and bladder)

C. **Low Dose Examinations** (exposure of gonads less than 10 mrad or mrem per average exam)

- Cervical spine (upper spine)
- Skull
- Shoulder
- Chest
- Dental (whole mouth or bitewing)
- Extremities (hands, feet, forearms, etc.)

See Appendices A and C for more details.

+ High category for females

* Medium category for females

TABLE 3: HIGH DOSES TO THE UTERUS AND FETUS

The following examinations of a pregnant woman may expose her unborn child to more than 4000 mrad or mrem:

Abdominal aortography (examination of the main arteries in the abdominal region)
Lower GI Series (barium enema)
Celiac angiography (examination of the blood vessels in the abdominal cavity)
Upper GI Series (barium swallow)
Hysterosalpingography (examination of the uterus and oviducts)
Pelvimetry (examination to measure the size of the pelvis)
Placentography (examination of the placenta)
Renal arteriography (examination of the kidney)
Urethrocytography (examination of the kidneys, urinary tract, bladder, and urethra)
Cystogram (examination of the bladder)

See Appendices A and B for more details.

TABLE 4: HIGH RISK CONTRAST X-RAY EXAMINATIONS *

Type of Study	Method	Uses
Bronchogram	dye injected into lung bronchi (air passages)	outlines bronchial tree
Cerebral angiogram (arteriogram)	dye injected into carotid and/or vertebral arteries in neck	outlines blood vessels in neck and brain
Coronary angiogram (arteriogram)	dye injected into chambers of heart	outlines heart chambers, valves, and surrounding arteries and veins
Pneumoencephalogram (PEG)	air injected (as per myelogram); air rises into brain	outlines chambers and surface of brain
Pulmonary angiogram (arteriogram)	dye injected into pulmonary arteries as they leave heart	outlines blood vessels (arteries and veins) in lungs

---

* Source: Arthur Levin, *Talk Back To Your Doctor* (New York: Doubleday, 1975).

A Word of Caution!

It is assumed that each and every x-ray examination adds directly to an individual's risk in proportion to the "effective dose" to which he or she is subjected. Although it is desirable to keep the total radiation dose received by a person as low as possible, it is important to realize that the risks associated with each proposed x-ray examination must be considered in light of the potential benefits of that same examination. Thus if a given x-ray examination appears necessary, a patient's past history of radiation exposure should not influence the decision to conduct that examination.

Don't forget to consider the substantial benefits of diagnostic x rays. GI examinations as part of an annual routine executive physical may be completely unnecessary. On the other hand, in the presence of certain symptoms, the information obtained from a relatively "high" risk GI examination may save your life! In such cases the risk of *not* having a GI examination is greater than the risk of the examination itself.

Avoid routine examinations or prescribing x-ray examinations for yourself. However, do not avoid an x-ray examination if your physician can adequately explain why ~~there is a~~ real need for it!

In spite of some of the shortcomings of certain dentists, physicians, and radiologists discussed in this book, a qualified professional is probably a better judge of when x rays are needed than you are. You have a right to expect any professional with whom you are dealing to provide complete answers to your questions about the need for a proposed x-ray examination. If, after reading Chapter 14, you feel that the practitioner's reasoning and diagnostic techniques are sound, you should abide by his or her judgment. If you are not confident about this judgment, by all means seek an independent one from another professional.

NOTES

Chapter 12

1. U.S., Environmental Protection Agency (ORP/SID) Publication 72-1, *National Radiation Exposure in the United States*, prepared by D. T. Oakley (Washington, D.C.: Environmental Protection Agency, June 1972), p. 42.

2. National Academy of Sciences, National Research Council, *The Effects on Population of Exposure to Low Levels of Ionizing Radiation* (BEIR Report), November 1972, p. 42.

3. International Commission on Radiological Protection Publication no. 8, *The Evaluation of Risks from Radiation* (New York: ICRP, 1966); *Ionizing Radiation Levels and Effects*, 1 and 2. *A Report of the United Nations Scientific Committee on the Effects of Atomic Radiation* (New York: United Nations, 1972).

4. R. Seltser and P. Sartwell, "The Influence of Occupational Exposure to Radiation on the Mortality of American Radiologists and Other Medical Specialists," *American Journal of Epidemiology* 81 (1965): 2–22; U.S., Bureau of Radiological Health, "Current Mortality Experience of Radiologists and Other Physician Specialists," prepared by G. M. Matanoski for the Division of Biologic Effects Seminar, 12 December 1973.

5. *The Evaluation of Risks*, pp. 4ff.

6. Ibid., p. 4.

7. W. M. Court-Brown and R. Doll, "Mortality from Cancer and Other Causes after Radiotherapy for Ankylosing Spondylitis," *British Medical Journal* 5474 (1965): 1327–32.

8. *The Effects on Population*, p. 68.

9. *The Evaluation of Risks*, p. 40.

10. A. M. Stewart and G. W. Kneale, "Radiation Dose Effects in Relation to Obstetric X Rays and Childhood Cancers," *Lancet* 1 (1970): 1185–88.

11. Irwin D. J. Bross and Nachimuthu Natarajan, "Leukemia from Low Level Radiation: Identification of Susceptible Children," *New England Journal of Medicine* 287 (1972): 107–10.

12. R. Gibson et al., "Irradiation in the Epidemiology of Leukemia Among Adults," *Journal of the National Cancer Institute* 48 (1972): 301–11.

13. U.S., Public Health Service (FDA), "X-ray Effects on the Embryo and Fetus: A Review of Experimental Findings," prepared by Robert Rugh and William Leach for the Bureau of Radiological Health (Rockville, Md.: Bureau of Radiological Health, September 1973), p. 2.

14. International Commission on Radiological Protection Publication 14, *Radiosensitivity and Spatial Distribution of Dose* (New York: ICRP, 1966), pp. 37ff.

15. Ibid., pp. 19–20.

16. *The Effects on Population*, chapter 5.

17. U.S. Department of Health, Education, and Welfare, *X-ray Examination—A Guide to Good Practice* (Rockville, Md.: Bureau of Radiological Health, 1971), p. 17.

Chapter 13

1. *The Consumers Union Report on Smoking and the Public Interest* (Mt. Vernon, N.Y.: Consumers Union, 1963), p. 34.
2. International Commission on Radiological Protection Publication 14, *Radiosensitivity and Spatial Distribution of Dose* (New York: ICRP, 1966), appendix 4, pp. 74ff.; National Academy of Sciences, National Research Council, *The Effects on Population of Exposure to Low Levels of Ionizing Radiation* (BEIR Report), November 1972, pp. 100ff.; *Ionizing Radiation Levels and Effects,* 1 and 2, *A Report of the United Nations Scientific Committee on the Effects of Atomic Radiation* (New York: United Nations, 1972), pp. 402ff.
3. W. Jacobi, "The Concept of Effective Dose Proposed for the Combination of Organ Doses," *Radiation and Environmental Biophysics* 12 (1975): 101–09; P. W. Laws and M. Rosenstein, "A Somatic Dose Index for Diagnostic Radiology," to be presented at the Twenty-Second Annual Meeting of the Health Physics Society (Atlanta, Ga.: 3–8 July 1977).
4. *The Effects on Population,* p. 91.
5. U.S., Environmental Protection Agency (ORP/SID) Publication 72–1, *National Radiation Exposure in the United States,* prepared by D. T. Oakley (Washington, D.C.: Environmental Protection Agency, June 1972), p. 42.
6. Arthur Levin, *Talk Back To Your Doctor* (New York: Doubleday, 1975).

APPENDIX A: UNITS OF RADIATION EXPOSURE AND DOSE

In order to understand how x rays interact with people, it is necessary to have some understanding of the ways in which scientists measure the quantity of x rays to which a person is exposed as well as the amount of x-ray energy or dose that person absorbs. Once the quantities associated with exposure and dose are defined, it is possible to discuss the potential effects of certain exposures or doses on human health.

Defining appropriate units to describe the effects of radiation has proven difficult for scientists ever since the discovery of ionizing radiation. As a consequence, three related units of radiation, each slightly different from the others, have been defined. Respectively known as the roentgen, rad, and rem, they are often used interchangeably in describing x rays that are striking an individual. This appendix is an attempt to describe important distinctions between these units of radiation.

Exposure and Dose—What Are They?

The effects of diagnostic x rays on the human body depend in a complex way on a number of factors such as the distribution of energies of x-ray photons in the beam, the total intensity or quantity of radiation, the distance between the x-ray tube and the individual being x-rayed, the type and location of tissues and organs in the main beam, as well as the age and sex of the person being examined.

In trying to understand the relationship between the properties of a given amount of radiation and the biological effect on an individual, the concept of exposure was developed. Exposure is a measure of the number of electrons which are torn away from molecules when a beam of radiation passes through air. A positively charged air molecule and the negatively charged electron removed from it are referred to as an *ion pair.* The concept of radiation exposure is very convenient since it is easy to place an ionization chamber containing air in the path of radiation and record the number of ion pairs produced by the beam electronically. The common unit of exposure is the roentgen, named after Wilhelm Roentgen who discovered x rays in 1895. One roentgen is the amount of radiation necessary to produce 1600 trillion ion (electron-molecule) pairs in one kilogram of air (1 kilogram=2.2 pounds).

Although the exposure in roentgens is an easy quantity to measure, it is not always a good indicator of the effects of radiation on an individual. This is because tissue, bone, and other materials contain different types of molecules and have different densities from air. Furthermore, the processes by which ionizing radiation like x or gamma rays, beta particles, or alpha particles lose their energy in passing through matter is different for each type of radiation. The energy absorption process also depends on the quality or energy distribution of the radiation as well as on the type of exposed tissue or bone.

The concept of *absorbed dose* was developed as a measure of the amount of energy dumped by incident radiation into a gram of material. The dose absorbed by a gram of skin or muscle can be much less than that of a gram of bone placed in the same x-ray beam. This is because the heavy atoms of calcium in bone absorb x rays more easily than lighter elements abundant in tissue. Thus x rays pass through tissue more easily and don't leave as much energy behind.

Absorbed dose, although harder to measure, is probably a better indicator of the biological impact of radiation than exposure. The most common unit of absorbed dose is the rad. Because the outer layers of material absorb x rays readily the exposure inside a person's body will be less than the exposure at the skin. The absorbed dose in the outer layers of skin is often referred to as the *skin dose* while x-ray energy deposited in a gram of bone, tissues, or an organ at a certain location inside the body is referred to as the *depth dose* at that location. High energy x-ray photons have much more penetration power, and the depth dose corresponding to a relatively high energy (100 kVp) diagnostic x-ray beam can be hundreds of times greater than that of a low energy diagnostic x-ray beam (20 kVp).

Since the exposure in roentgens is the same as the absorbed dose in rads at the surface of soft tissue for medical x rays, these units are sometimes used interchangeably. *However, in most situations a measurement of x-ray exposure in roentgens made with an ion chamber at the surface of the body is not the same as the dose or energy absorbed at various points in the body in rads.* When other types of radiation like alpha particles or neutrons are present, a unit called the rem is used. Rem stands for Roentgen Equivalent Man and describes the potential for biological damage which results from a given dose in rads of radiation other than x rays. *However, for x rays, rad and rem always have the same value and can be used interchangeably.*

At present most researchers studying the biological effects of ionizing radiation on humans assume that its effects on a particular location in a body can be directly related to the absorbed dose in each gram of material at the location of interest. However, some effects of interest may be related to the time period in which the dose is observed, or *dose rate,* as well as the total absorbed dose. Very high dose rates are known to do more somatic damage to individuals than the same total dose delivered more slowly. The relationship between genetic and somatic damage and dose rates for lower doses is not well established, and it is safer in setting radiation standards to assume that biological effects depend only on total absorbed dose (except at very high dose rates).

The concepts of absorbed dose and dose rates are very powerful and useful. Our present state of knowledge is such that if an individual absorbs a known dose at each location in his body within a specified amount of time, it is possible to set upper limits using the linear hypothesis on the effects the radiation will probably have on his health.

APPENDIX B: EXPOSURES TO EMBRYO AND FETUS

Range of Possible Exposures of an Embryo or Fetus in Various X-ray Diagnostic Procedures of the Pregnant Woman *

Diagnostic Radiography	Dose Range in Millirads
Abdomen screening	100-2000 depending upon whether there are multiple films and/or fluoroscopy
Abdominal aortography *	6,000-20,000
Amniography	100 or more depending upon techniques used
Barium enema *	350-6,000 (higher with fluoroscopy and spot film)
Carcinoma of the cervix	To 6,000 if fluoroscopy is used
Cardiac series	5-50, higher with fluoroscopy
Celiac angiography *	2,000-20,000 (with fluoroscopy)
Cephalopelvimetry	See pelvimetry
Chest	Single view 1-10 or less; 5-70 or to 2,000 with fluoroscopy
Cholangiography	20-200 (films) or to 2,000 (fluoroscopy)

---

* Denotes procedures which are high risk to the fetus because they may deliver 4 rads or more to it.

Cholecystography	20-200 (films) or to 2,000 (fluoroscopy)
Cystogram (excluding urethra)	500-1,000
Colon	See GI series, lower tract
Dacryocystography	1-10
Dental series	0 with lead and rubber apron
Esophagram (esophagogram)	To 500 with fluoroscopy
Extremities	Negligible (1 mrad)
Femoral arteriography	1,000+
Fetal age	500-1,000
Fetometry	100-300
Gallbladder	See cholecystography
GI series, lower tract *	350-6,000, higher exposure with fluoroscopy
GI series, upper tract	100-2,000, higher exposure with fluoroscopy
Hip (spine and buttocks)	300-700
Hysterosalpingography *	1,200-6,000. Rarely involves pregnancy, upper exposure levels with radiopaque and fluoroscopy
Ileo-cecal study	100-2,000, higher exposure with fluoroscopy
Intestine, small study	100-1,000 with multiple films and fluoroscopy
K.U.B. (kidney, ureter, and bladder)	200
Long bone series	50-200
Mastoid areas	25-100
Myelography	Minimum of 2,000 spot films and fluoroscopy
Nephrotomography	500-2,000

---

* Denotes procedures which are high risk to the fetus because they may deliver 1 rads or more to it.

Obstetric examinations	500-2,000 if laterals and stereo included
Ocular foreign body detection	1-10
Pelvic pneumography	300
Pelvic, lower abdomen screen	80-500
Pelvimetry *	600-4,000 (usually toward term)
Petrous pyramids	1-10
Placenta praevia	500-1,000 with contrast injection
Placentography *	300-7,500 with contrast injection
Pneumoencephalography	2-20
Polytomography (both ears)	3-30
Prenatal mortality detection	100-500
Pyelography, intravenous	400-2,000, multiple films and radio-opaque
Pyelography, retrograde	450-1,000, multiple films and radio-opaque
Renal arteriography *	2,000-4,200
Retroperitoneal study	500
Salpingography	10-50
Sella turcica	1-5
Shoulder	Negligible
Sialography	1-10
Sinus series	1-10 (paranasal)
Skeletal series for metastases	50-200
Skeletal maturity detection	Negligible (one hand, one knee, or more)
Skull series	1-10 (av. 4)
Spine, lumbar (sacrum and coccyx)	214-2,000 with lateral and oblique views
Splenoportography	2,000
Small intestine survey	500-1,000 (without fluoroscopy)

---

* Denotes procedures which are high risk to the fetus because they may deliver 4 rads or more to it.

Temporo-mandibular joints	1-10
Urethrocytography (like K.U.B. and cystogram but includes urethra)*	To 600 with films, to 6,000 with fluoroscopy, and to 20,000 with cine
Venocavography	1,000+
Ventriculography	2-20

Major References for Table of Diagnostic Radiography**

Bewley, D. K., Laws, J. W., and Myddleton, C. J., 1957. Maternal and fetal radiation dosage during obstetric radiography examination. *Brit. Journ. Radiology* 30:286-290.

Brent, R. 1960. The effect of irradiation of the mammalian fetus. *Clinical Obstetrics and Gynecology* 3:928-950.

Brent, R. 1972. Irradiation in pregnancy, In *Gynecology and Obstetrics*. Davis, ed. 32:1-30 Harper and Row.

Brown, M. L. 1965. Population dose from x rays. PHS Pub. #2001. ICRP-ICRU, 1969. Exposure of man to ionizing radiation arising from medical procedures with special references to radiation induced disease. An inquiry into methods of evaluation. *Physics in Medicine and Biology* 6:199-258.

Kinlen, L. J. and Acheson, E. D. 1968. Diagnostic irradiation. Congenital malformations and spontaneous abortion. *Brit. Journ. Radiology* 41:648-654.

Michigan Survey. 1961. Medical Radiological Health Data, "Michigan survey of medical radiology experience during pregnancy." 2:159-164.

Peter Bent Brigham Hospital Report. Peter Bent Brigham Hospital, 721 Huntington Ave., Boston, Mass., 1964.

Reekie, D. and Davison, M. 1967. The radiation hazard in radiography of the female abdomen and pelvis. *Brit. Journ. Radiology* 40:849-854.

Schwartz, Gerhard, M.D., Director, Department Radiology, New York Eye and Ear Infirmary, also Fellow American College of Radiology (FACR), Clinical Professor of Radiology, New York Medical College, Practice 33 years. (Consultant on table of exposures to the fetus.) Personal communication, 1972, 1973.

---

* Denotes procedures which are high risk to the fetus because they may deliver 4 rads or more to it.

** This list was obtained from a paper entitled:
"X-ray Effects on the Embryo and Fetus: A Review of Experimental Findings" by Robert Rugh and William Leach, Division of Biological Effects, Bureau of Radiological Health, FDA, United States Public Health Service, Rockville, Maryland 20852 (September 1973).

APPENDIX C: AVERAGE DOSES FOR TYPICAL X-RAY EXAMINATIONS IN MILLIRADS

	Average skin dose per film (a)	**Average integral bone marrow dose per exam (b)**
Mammography	1500†	—
Upper GI	710	300
Thoracic Spine	980	200
Lower GI	1320	600
Lumbosacral Spine	2180	200
Lumbar Spine (LS)	1920	200
Intravenous Pyelogram (IVP)	590	300
Cervical Spine	240	50†
Cholecystography	620	100
Abdomen or KUB	670	100
Skull	330	50
Lumbo-pelvic	610	100
Chest (radiographic)	44	40
Dental (whole mouth)	910	20
Hip or Upper Femur (thigh)	560	100
Shoulder	260	50†
Dental (bitewing)	920	4
Extremities	100	<10

References

(a) U.S., Department of Health, Education, and Welfare (FDA) Publication 73-8047, *Population Exposure to X rays U.S. 1970*, (Rockville, Md.: Public Health Service, November 1973). Appendix III.

(b) International Commission on Radiological Protection Publication no. 16, *Protection of the Patient in X-ray Diagnosis* (New York: Pergamon Press, 1970).

Average no. of films per exam (a)	**Estimated "effective" dose per exam (c)**	**Average gonadal dose per exam (d)**	
		M	**F**
2*/per breast	300-600	—	—
4.3	150-400	30	150
3*	150-400	<10	<10
2.9	90-250	200	800
3.4	70-250	1000	400
2.9	50-180	1000	400
5.3	50-150	1300	800
3.7	40-80	<10	<10
3.3	25-60	5	150
1.6	10-60	500	500
4	20-50	<10	<10
1.4	5-35	700	250
1.6	5-35	<10	<10
16*	10-30*	<10	<10
3*	2-25*	1200	500
2*	2-25	<10	<10
3*	<5*	<2	<2
2.7	<5*	<10	<10

(c) Preliminary estimates based on work in progress: P. W. Laws and M. Rosenstein, "A Somatic Dose Index for Diagnostic Radiology," to be presented at the Twenty-second Annual Meeting of the Health Physics Society (Atlanta, Ga.: 3-8 July 1977).

---

† *Ionizing Radiation: Levels and Effects,* 1, *A Report of the United Nations Scientific Committee on the Effects of Atomic Radiation* (New York: United Nations, 1972), pp. 162, 164.

* Estimate by author.

DOSES FOR TYPICAL X-RAY EXAMINATIONS

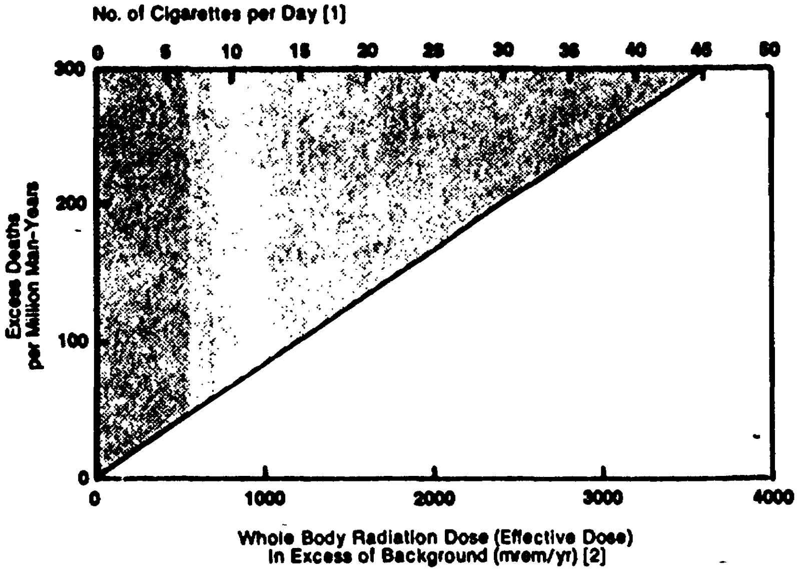


Fig. 1 — Comparison of excess deaths from lung cancer due to cigarette smoking and estimated average excess deaths from leukemia and cancer due to exposure to diagnostic x rays and other ionizing radiation

---

1. *The Consumers Union Report on Smoking and the Public Interest,* (Consumers Union, Mt. Vernon, N.Y., 1963), p. 34.
2. National Academy of Sciences, National Research Council, *The Effects On Population of Exposure to Low Levels of Ionizing Radiation* (BEIR Report), November, 1972, p. 91.

APPENDIX D: PERSONAL RADIATION RECORD—DIAGNOSTIC X-RAYS

Name .... Sex ....

Address .... Birthdate ....

Date	Physician or Dentist	Location of x-ray facility	Type of Examination	Estimated effective dose*	Estimated gonadal dose*	Details (shielding, mAs, filtration, kVp, etc.)	Purpose of x-ray examination

* See Appendix C for estimate of doses for various procedures conducted under average conditions.

Mr. Rogers. Thank you very much, Dr. Laws. We appreciate your comments and suggestions.

Dr. McClenahan.

STATEMENT OF JOHN L. McCLENAHAN, M.D., PHILADELPHIA, PA.

Dr. McClenahan. Mr. Chairman, I prepared a seven-page statement that I have submitted giving my views on overutilization of X-rays. When I read it on the train coming up this morning, it seemed a little windy. With your permission, I will simply extract it and speak from my notes.

Mr. Rogers. You are welcome to do so Doctor, thank you.

Dr. McClenahan. A word of background, I am a doctor, and M.D., graduate of Yale University and the University of Pennsylvania Medical School. I served an internship in Philadelphia, a residency in radiology at the New York Hospital-Cornell Center in the Department of Radiology. I remained for 4 or 5 years after my training when I tired of institutional radiology and was conscious of a widening distance between myself and patients.

I moved back to my home in Philadelphia, opened a small office in the country in suburban Philadelphia where I have practiced for 22 years. The only distinction I bring to a hearing such as this is small: I see each patient who comes to me; I question them; I examine them; I specifically order which examinations are to be done and are not to be done. I reserve the right to veto an examination or to curtail it if necessary.

When I am not in my office, no work is done. Today, my staff is on a picnic in Fairmount Park.

It seems to me that one of our principal problems in this entire discussion is the widening distance between radiologists and their patients. This has been spoken of obliquely in earlier testimony but it is the main burden of my talk this afternoon.

In spite of efforts to curtail and to reduce examination and constantly to wonder why it was being done—in spite of this supervision—in the past 22 years, a great deal of my work has been done for reasons of doubtful need, in my opinion, and I have contributed my share of unnecessary X-ray exposure.

It is possible to argue about the word "unnecessary"; it can be debated for hours. In the present discussion, I take it to mean an examination done for purposes other than the quest for an anatomical or physiological diagnosis, regardless of how the examination may be justified.

The number of excessive procedures, I think, is relatively large; the number of doctors that make them possible, I think, is relatively small.

I consider the following examinations unnecessary: First, routine studies that are requested, ordered, to determine whether a patient without symptoms is, in fact, in good health. These, for the most part, are screening procedures of the chest and other organ systems, undertaken as part of a so-called complete checkup and paid for under a fringe benefit.

Second, examinations done to exclude injury after a trifling injury where there is a question of liability.

Third, examinations done to allay anxiety in a patient suffering from vague or transient malaise or anxiety in the relative of such a patient.

Fourth, examinations done to allay anxiety in physicians who require it as at least a token protection against a possible charge of negligence.

Fifth, examinations done to rule out. These are ordered when the diagnosis has been made with reasonably certainty on the basis of history and physical examination. There seems to be a reluctance to ascribe symptoms to a single cause; the diagnosis seems too obvious to be believed. I becomes necessary to exclude theoretical causes of discomfort.

For example, a patient with classical symptoms of a kidney stone will be subjected to X-ray examinations not only of his kidneys but of his spine, chest, colon, stomach, and gall bladder to determine to what extent these organs may be contributing to his disability.

Sixth, to document improvement that is clinically apparent. If, for example, an individual's abdominal pain and indigestion improve after treatment, a gastrointestinal series may be ordered to determine whether or not his duodenal ulcer has diminished in size.

Other debatable uses of diagnostic X-rays occur more frequently in institutions than in offices. Those that I have observed include the following: Seventh, examinations ordered to embellish a diagnosis that is certain; to satisfy curiosity.

If, for example, it has been established that a tumor has spread to one distant bone or organ, studies are commonly ordered of all the bones and all the distant organs, even those not clinically involved, together with selective isotope scans and, more recently, computerized tomographic scans.

These are inrteresting but their role in patient management or in the maintenance of comfort can be seriously doubted.

Eighth, uselessly repeated examinations. In teaching institutions particularly, parochial concepts of technical adequacy denigrate the contributions of outsiders. A patient may report to a counsultant carrying an armload of X-ray films and a radiologist's report concisely summarizing what they show. The consultant may not even glance at these before putting them aside and ordering a new set of identical studies in his own X-ray department.

Ninth, examinations are undertaken as part of self-referral and this, Sir, I believe is the most serious cause of X-ray over utilization.

Radiologists—occasionally resort to it. Nonradiologists who own their own apparatus find it hard to resist. Whatever his specialty or general practice, a self-referrer reports only to himself. It is virtually impossible to monitor the quality or quantity of his work. Third parties pay him the same fee for X-ray services that they pay to an expert. His competence is never tested. His understanding of radiation hazards and hygiene is rudimentary. For purposes of economy, he frequently relies on the fluoroscope, a cheap, impressive, dangerous source of radiation.

Perhaps, I could suggest just a few methods that I believe would reduce overutilization of diagnostic radiology in our country. Some of them you have already heard. I think it would be of value to eliminate all third-party payment for routine survey screening X-ray examinations except in instances where there are bonafide symtoms or a family history of congenital diseases accessible to radiological scrutiny.

For example, it would be permissible to screen an individual with a family history of breast cancer or polycystic disease of the kidneys. It would not be justifiable to screen an individual with coronary artery disease or diabetes mellitus in family antecedents.

I think another great help would be to make thrift less risky. Current penalties for error in the practice of medicine are harsh and there is no forgivness. Restraint in ordering X-rays is never rewarded. Extravagance is never punished. It is natural for doctors to protect themselves by ordering excessive tests even when these may be only symbols of thoroughness. The cost of one contrary legal judgment can bankrupt a conscientious physician who has failed, just once, to order a single X-ray examination, out of concern for undue cost or undue X-ray exposure.

What can be done to dispell the illusion of costliness? To patients, who have come to be called consumers, third-party treasuries are distant and their resources inexhaustible. An incentive plan that offered material reward for reduced demand of benefits would reduce excessive X-rays. It should be possible to progam a computer to reject automatically payment of a bill for examination repeated within a predetermined time, leaving the proof of its need up to the party making the second claim.

I would strongly recommend any measure to discourage self-referral. In rural communities with limited X-ray facilities, doctors have no choice but to use their own machines. But where adequate professionally staffed, radiological services exist, self-referral amounts, in fact, to fee-splitting with one self. It is hard to control such a breach of ethics. As a matter of fact, most of what we are speaking of today, I think, comes under the heading of ethics and morality rather than simple legislation.

Some restraint might be possible by strict enforcement of safety standards and by spot monitoring of films and records by a regulating agency.

I think efficiency could be greatly encouraged in the use of X-rays by fostering competition. For years, as many of us know, some insurers have refused to pay for diagnostic radiology performed in an office even when the service was rendered by a radiologist with the highest qualifications. Reimbursement is made for identical service performed in a hospital without question. And yet the cost of most examinations in a hospital is more than the cost in an office by a factor of some 50 to 200 percent. These restrictions are capricious and discriminatory, adding to the cost of medical care and opening the way to fraud, by the admission of patients to hospital beds in order to make them eligible for diagnostic service.

Reimbursement for X-ray diagnoses should be based on professional merit and not on geography.

Finally, responsibility for the proper use of X-ray lies on the shoulders of radiologists who are, as they declare, physicians trained in the safe use of radiation. As physicians, it follows that they must be willing to cope with sick people, to approach them, to evaluate every request that comes into their hands in terms of the circumstances that exist, to challenge and have courage to reject casual requisitions and limit their every examination to as few exposures as will suffice for a diagnosis.

To do this will require some practice and some time but, on the whole, less time than frantic and occasionally aimless overactivity, and the investment will yield greater safety and economy.

Thank you, sir.

Mr. ROGERS. Thank you very much, Doctor, for a very helpful statement. Do I understand that you are saying that it is not a normal practice for a radiologist to share in the determination as to whether an X-ray should be given?

Dr. MCCLENAHAN. It is occasionally done. As a general rule, the requisition is submitted to a department and it is seen by a technician. It may be seen by a radiologist, but it is very commonly the practice that the radiologist does not know the examination has been done until he sees the films.

Mr. ROGERS. Thank you.

Dr. Allan B. Reiskin, professor of radiology, Department of Oral Diagnosis, Division of Oral Radiology, University of Connecticut, School of Dental Medicine, we welcome you. You may proceed as you desire.

STATEMENT OF ALLAN B. REISKIN, D.D.S.

Dr. REISKIN. Thank you, Mr. Chairman, members of the committee. Thank you for the opportunity to participate in these hearings. I am going to attempt to do a little adlibing so I do not repeat material which has already been presented [see p. 61].

I think my chief concern centers around my observation that the level of education and training received by most dentists and their assistants is inadequate. My colleagues are, to the best of my knowledge, conscientious and careful and they practice at or near the level of their competence, but I think it is important to emphasize and to recognize that their training is not extensive.

Up to the present decade, most radiobiological literature dealt with laboratory-type experiments using relatively high levels of exposure. Information on the response of human subjects to ionizing radiation was limited to patients who were therapeutically irradiated with large doses because of serious underlying disease or to individuals who were exposed as a result of nuclear accidents and detonations.

The ability of X-rays to produce a variety of pathological changes, including cancer, became evident very early, but it was presumed that the induction of cancer and other such effects required extremely large doses of radiation well beyond the range of those which are used in diagnostic radiology.

Unfortunately, that presumption still determines the actions and practices of many dentists. The doses which have most recently been associated with an increase in the spontaneous incidence of malignant disease are clearly within the diagnostic range and I am referring, in particular, to some reports which appeared within the last few months and review data on workers at the Hanford, Washington plant and the shipyards in Portsmouth, N.H.

Experiments have also shown that low levels of exposure to ionizing radiation can enhance the tumor-inducing potential of many agents including polycyclic hydrocarbons and viruses, many of which are commonly found in the mouth and respiratory tract.

The ability of X-rays to demonstrate carious lesions in teeth and diseases of the tooth-supporting structures is so impressive and these pathological changes are so prevalent that virtually every dentist owns and uses an X-ray machine. The need to conduct examinations is taken for granted and, as we have already been told, can involve serious abuse when it comes to self-referral since the dentist is his own radiologist.

By way of background, in 1964-70, the Public Health Service conducted studies on population exposures. The Public Health Service study indicated that in 1970, 59.2 million persons were X-rayed for dental purposes. The report stated that dental exposures approached a peak rate of almost 40 per 100 population at the age of 25, that more females were exposed than males, that the rate of exposure was highest in the West and lowest in the South, and the rate of exposure increased with family income and with education, but decreased with age after the peak incidence.

Sixty-seven and one-half percent of all dental visits included X-ray exposure compared to 28 percent of visits to a physician's office. Seventy-eight examinations or procedures were conducted using an estimated 286 million films; that is in 1 year.

The average mean exposure per film was considerably lower than had been previously estimated but was still significant at 910 milliroentgens. A dental X-ray is clearly one of the most common types of radiographic examinations in use today. It is estimated that there are more than 143,000 dental X-ray units in use in this country.

A recent survey of practices in American dental schools indicated that essentially every school requires an X-ray examination of every patient prior to treatment and more than half of the schools require multiple examinations of the same anatomical sites by different X-ray techniques.

There was only one institution that, as a matter of policy—I regretfully add not practice—advocated limiting exposures to those required as a result of a clinical examination of the patient and a careful history.

In practice, if not in policy then, dental schools teach students to use X-ray examinations as a routine screening procedure, contrary to the recommendations of the BIER report, the American Dental Association, the American College of Radiology and a variety of other groups.

In the private sector, Crabtree and his colleagues reported the results of a survey conducted in Nashville, Tenn. Their survey pointed out that 50 percent of all offices perform limited examinations every year on all patients, while 21 percent comprehensive examinations every 1 to 3 years.

Sixty-four percent of the offices selectively did a full-mouth series which might include up to 21 films on all new patients, and 58 percent routinely conducted interproximal examinations.

These data suggest a pattern of overutilization which may be related to the basic education of practitioners.

Subsequent studies by Gibbs & Associates indicated that consideration of professional judgment in the ordering of radiographic examinations appeared to have gained better acceptance with continuing education, but the same study showed that excessive exposures resulting from poor technique persisted.

X-ray examination is only of value when the resulting radiographs are of readable quality. An evaluation of preauthorization radiographs submitted to Pennsylvania Blue Cross indicated that two-thirds of the films were inadequate as a basis for determining the efficacy of a proposed treatment plan. That is rather astounding.

Detailed studies demonstrated that between one-half and three-quarters of the radiographs examined were technically unsatisfactory and there is little reason to believe that the sample obtained in Pennsylvania is different from the experience that might be encountered by a similar survey in other parts of the country.

In my prepared statement, there is a fairly extensive breakdown of the costs that are involved in performing X-ray examinations and I think I will summarize it by simply saying that radiography is a profitable part of practice, certainly as profitable as other activities and perhaps more profitable. That may be partly responsible for some of the difficulties.

At the heart of the problem is the issue of education. Surveys of instructional programs in dental radiology were conducted through the years 1967 to 1977. The initial survey was done by Greer and his associates with the support of the Bureau of Radiological Health and it looked at the qualifications and training of radiology faculty members.

The report produced a profile of the average teacher of dental radiology as a 44-year-old male who had been teaching for 12 years. His dental degree was his highest degree, and he was entirely self-taught with only intermittent attendance at courses in radiology. He had very limited background in research and devoted only about one-half of his professional time to radiology.

He spent about an average of 2.5 hours in research and may or may not have published a single research paper in a 5-year period.

On the average, there were 1.4 full-time equivalent teachers of radiology for schools having 100 students in a class. One school had one person who devoted 5 percent of his total professional time to teaching 123 students, while at the opposite extreme, another school had three people teaching dental radiology 80 percent of their time to 50 students.

Only four schools in the United States met the recommended staffing levels advocated by the American Association of Dental Schools. Most of the schools had faculty student ratios lower than 0.02 with the majority of schools having even fewer full-time equivalent instructors per 100 students.

The B.R.H. study also looked at the total amount of curriculum time which was devoted to radiology and, being charitable, they came up with a range of from 26 to 288 hours of total time expended on instruction in radiology.

I think that in most hospitals, a radiologist would be reluctant to hire a technician who has not had at least 2 years of formal training.

A more recent survey published in 1977 contained data which was not significantly different from the earlier study. Most dental schools were found to offer from 10 to 30 clock hours of didactic material in the first or second year and from 1 to 20 hours later in the curriculum.

Few schools reported courses longer than 30 hours in a single block.

There have been a few important improvements in X-ray generators and films, but the pattern of X-ray utilization in dentistry has not changed substantially in the last few decades.

By contrast, the acceptance of radiology as a specialty in medicine has lead to fairly impressive and positive changes. In dentistry, new devices which can provide substantial reductions in exposure are rarely used. Because most dental care is provided by individuals who work in isolation from their colleagues, there is very little opportunity for peer review.

The advent of third-party payment plans has broadened the distribution of dental care and has also provided a vehicle for examining both the pattern and quality of care as was illustrated by the Pennsylvania Blue Cross study.

In summary, I do not feel that there is any conspiracy among my professional colleagues to cause injury to the population by injudicious overutilization of X-rays, but I think there is a major problem which results from inadequate education. I believe the evidence strongly indicates that there is both overutilization and overexposure. Unfortunately, the problems associated with the dissemination of radiobiological information and the political and economic forces which bear on us as professionals seem to mitigate against change and to support the status quo.

Regretably, I suspect that without some outside intervention, changes will occur very slowly.

[Testimony resumes on p. 74.]

[Dr. Reiskin's prepared statement follows:]

STATEMENT OF
DR. A. B. REISKIN
PROFESSOR OF RADIOLOGY, DEPARTMENT OF ORAL DIAGNOSIS
SCHOOL OF DENTAL MEDICINE, UNIVERSITY OF CONNECTICUT
BEFORE THE
SUBCOMMITTEE ON HEALTH AND THE ENVIRONMENT OF THE
COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE
JULY 11, 1978

MR. CHAIRMAN AND MEMBERS OF THE SUBCOMMITTEE:

I am Dr. Allan Reiskin of Avon, CT., a professor of radiology at the School of Dental Medicine at the University of Connecticut. I am pleased to provide the Subcommittee with background material on the possible hazards associated with low level exposures to ionizing radiations used in dental x-ray diagnosis. My curriculum vitae has been made available to the Subcommittee and provides a detailed description of my background. Briefly, before joining the faculty of the University of Connecticut I was employed at the Atomic Energy Commission's Argonne National Laboratory as an associate biologist. My dental training was received at the University of Pennsylvania and my training in radiation biology, radiologic physics and related radiologic sciences was received at the University of Pennsylvania Graduate School of Medicine and at the University of Oxford. My main professional interests have been radiation toxicity, specifically, radiation carcinogenesis and radiation dose reduction in diagnosis.

It is my opinion that recently published data on the risk of adverse effects from exposure to ionizing radiation is not well known among my colleagues in dentistry and that it has not been given adequate attention in the definition of indications for x-ray examination. This is the result of benign neglect within our professional community. Although x-ray diagnosis is considered to be an essential component of dental practice, radiology has never been given the recognition accorded to other dental specialities and it rarely has a position of prominence in dental curricula. Many continuing education programs are superficial, dealing primarily with problems of film placement and patient positioning but with little attention to physics, photochemistry, radiation biology, or principles of diagnosis.

Available data indicate that a significant number of routine dental diagnostic x-ray procedures are unnecessary and that the exposures used in these procedures are frequently larger than would be afforded by state-of-the-art techniques. Over exposure and over utilization occur because of inadequate education and the lack of meaningful guidelines or controls.

In many parts of the country, x-ray procedures are performed by dental assistants who have little or no formal training in x-ray technology. As a result, there is little capacity for minimizing technical errors and little awareness of biological effects. Furthermore, because the adverse effects of low level exposure are 'late effects' and there is no immediate response in the patient, the concern and the perceived responsibility of the operator and/or dentist are diminished. Although a number of techniques are available for reducing the level of exposure per film and per examination, few of these techniques are taught in dental or dental assistant schools and they are rarely used in most practices.

The basis for my opinions is outlined in the body of my statement. The data is taken from the scientific literature, much of which has already been presented to this and other Congressional committees. In the long term, improvement of practice standards will require substantial upgrading of our educational system. It is important to recognize however, that a decision to expand the radiology curriculum in dental schools could not be readily implemented because of the extremely small number of qualified teachers. Therefore, in the short term, it may also be necessary to regulate the use of diagnostic x-ray equipment.

As a practitioner of dentistry I would prefer to see professional standards established by the providers of dental care. As a consumer I am concerned that standards established by the profession are not adequately implemented.

Background - Risks and Ionizing Radiation

In 1972 the report of the Advisory Committee on the Biological Effects of Ionizing Radiation (BEIR) called attention to several important issues and in particular, to the need for considering somatic as well as genetic effects in the development of risk estimates and cost/benefit ratios related to radiation exposure. The assumption that the genetic risks from low-level exposures to ionizing radiation were of greater importance that the somatic risks was rejected on several accounts. Available biological data suggested that the induction of cancer by radiation was a linear, non-threshold process. Using these premises, risk estimates were calculated from data recorded from the A-bomb survivors of Hiroshima and Nagasaki as well as from patients who were therapeutically irradiated and from individuals who were occupationally exposed. The calculated estimates suggested that exposures of 5 rem per thirty years could cause between 3,000 and 15,000 cancer deaths annually or approximately a 2% increase in the spontaneous cancer death rate.

Although the BEIR report evolved from a concern over the increased use of nuclear energy and the need to re-evaluate associated radiation protection policies, the report also concerned itself with exposures from medical and dental applications. It pointed out that medical and dental exposures were not under any control or guidance by regulation or law, and recommended that exposures from medical and dental uses should be evaluated according to the same criteria used for other types of man-made exposures. The report indicated that in the foreseeable future radiation exposure from natural background and medical applications would continue to constitute the major contribution to population exposure. The report emphasized that exposures should be reduced in all instances where they did not impair diagnostic benefit. Specifically, the BEIR report recommended: "No exposure to ionizing radiation should be permitted without the expectation of a commensurate benefit; the public must be protected from radiation but not to the extent that the degree of protection provided results in the substitution of a worse hazard for the radiation avoided. Additionally, there should not be attempted the reduction of small risks, even further, at the cost of large sums of money that spent otherwise, would clearly produce greater benefit; medical radiation exposure can and should be reduced considerably by limiting its use to clinically indicated procedures utilizing efficient exposure techniques and optimal operation of radiation equipment. Consideration should be given to the following: (1) restriction of the use of radiation for public health survey purposes, unless there is a reasonable probability of significant detection of disease; (2) inspection and licensing of radiation and ancillary equipment; (3) appropriate training and certification of involved personnel."

It is extremely difficult to assign any precise level of risk to the radiation exposure which results from dental examinations. One approach to estimating risk might involve examining the impact of a specific level of exposure on a target tissue such as the active bone marrow. The bone marrow is more radiation-sensitive than many other organs and the latent period for cancer induction is relatively short. From several available models, Ellis, Healy, Shleien, and Tucker (DHEW Publication (FDA) 76-8015) used data developed by Custer which indicated that in a 40-year-old, approximately 13% of the active marrow lies within the head. In younger individuals, one may presume that the percentage of active marrow in the head and facial skeleton is higher. Recent studies by Mancuso, Stewart and Kneale and Najarian and Colton provide estimates of the risk of radiation-induced leukemia. The data is wide-ranging but establishes significantly greater dose response relationships than had been previously recognized. (In one instance, an exposure of .211 rem annually of whole body exposure appeared to account for an increase in the mortality of leukemia and all cancers expected for U.S. white males of the same age groups. In another instance, whole body exposures of approximately 0.8r were estimated to increase the incidence of naturally-occurring leukemias.) Although this data is controversial and relates to whole-body exposures, it substantially reduces our estimate of what constitutes a significant exposure. Furthermore, if one can assume that ten units of radiation to 10% of the active marrow is equivalent to one unit of radiation to 100% of the active marrow, then the significance of exposures used in dentistry increases and will grow with the expansion of dental services. The capacity for low levels of ionizing radiation to induce tumors has also been demonstrated in the thyroid gland.

Utilization

In 1964 and in 1970, the Public Health Service conducted studies of population exposures to x-rays. The resulting reports contained data on patterns of utilization which are relevant to issues raised by the BEIR report and primarily to the concern that medical and dental uses be evaluated by appropriate cost/benefit parameters. The PHS study indicated that in 1970 59.2 million persons were x-rayed for dental purposes. The report also stated that dental exposures approached a peak rate of almost 40/100 population at the age of 25; that more females were exposed than males; that the rate of exposure was highest in the West and lowest in the South; that the rate of exposure increased with family income and with education but decreased with age after the peak incidence. Sixty-seven and a half percent of all dental visits included x-ray exposure compared to 28% of visits to a physician's office. Seventy million dental examinations or procedures were conducted using an estimated 286,000,000 films. The average mean exposure per dental film though lower than the 1,138 mR estimated in 1964, was still significant at 910 mR.

A dental x-ray is one of the most common types of radiographic examinations in use today. There are probably more than 143,000 dental x-ray units in use in the United States. A recent survey of diagnostic practices in American dental schools indicated that essentially all schools require x-ray examinations of all patients prior to treatment while almost half of the schools require multiple examinations of the same anatomic sites by different techniques. Only one institution, as a matter of policy (but not practice), advocated limiting exposures to those required as a result of clinical examination and history. In practice, if not in policy, dental schools teach students to use x-ray examinations as a routine screening procedure contrary to the recommendations of the BEIR report, the American Dental Association, the American College

Radiology, and the Environmental Protection Agency's Interagency Working Group on Medical Radiation. In the private sector, Crabtree et al. reported the results of a dental radiography survey conducted in Nashville, Tennessee. This survey pointed out that 50% of the offices performed limited examinations every year on all patients while 21% did comprehensive examinations every one to three years. Sixty-four percent of the offices selectively did a fullmouth series on new patients and 58% routinely conducted interproximal examinations. These data suggest a pattern of over-utilization which may be related to a practitioners basic educational experience. Subsequent studies by Gibbs et al. indicated that considerations of professional judgement in the ordering of radiographic examinations on new patients and repeat examinations on regular patients appeared to have gained better acceptance with continuing education. Unfortunately, the same study indicated that excessive exposure resulting from poor technique persisted.

Quality

X-ray examination is of value only when the resulting radiographs are of interpretable quality. An evaluation of preauthorization dental radiographs submitted to Pennsylvania Blue Shield indicated that two-thirds of the films were inadequate as a basis for determing the efficacy of proposed treatment plans. Detailed studies demonstrated that between one-half and three-quarters of the radiographs examined were technically unsatisfactory. There is little reason to believe that the sample obtained in Pennsylvania is dramatically different from the experience that might be encountered in other parts of the country.

Cost

The cost of a dental x-ray unit may vary from approximately two to five thousand dollars for a conventional unit and from nine to thirteen thousand dollars for curved surface tomographic(panoramic)units. The typical x-ray unit should operate for a period of 20-30 years with minimal maintenance so that the annual cost distributed over the useful lifetime could be as low as one to three hundred dollars per year. The cost of film for intraoral examinations ranges from approximately nine to fifteen cents per film or a maximum of approximately three dollars for the most comprehensive type of dental examination. In the State of Connecticut, it has been estimated that 90% of the radiographic examinations are performed by dental assistants with no formal training in radiology. The labor cost involved in completing the examination is usually low and can be estimated at approximately two to five dollars per examination depending on the pay scale of the operator. Processing expenses are negligible, contributing less than a dollar to the operation. A typical office may conduct up to approximately ten complete examinations a week or up to 500 per year so that the average capital expenditure can be estimated at about one dollar. Making some allowance for indirect expenses, one might conclude that the overall cost for conducting an examination would be under ten dollars. The mean fee for a complete intraoral exam at the time of the last American Dental Association survey was $22.11 which suggests that the direct and indirect costs for a radiographic examination are approximately one-half or less of the established average fee. This would appear to be consistent with fee patterns in other areas of the health care industry and might be reasonable compensation for professional service if there were evidence to indicate a high diagnostic yield and effective utilization.

Faculty, Facilities and Curriculum in Dental Radiology

Surveys of instructional programs in dental radiology were conducted in the years from 1969 thru 1977. The initial survey was conducted by Greer et al. with the support of the Bureau of Radiological Health and examined the qualifications and training of dental radiology faculty members and their facilities. This report produced a profile of the average teacher of dental radiology as a 44-year-old male who had been teaching for 12 years. His dental degree was his highest degree and he was entirely self-taught with intermittent attendance at courses in radiology (most of which are technically oriented). He had a very limited background in research and devoted about half of his professional time to radiology. He spent an average of two-and-one-half hours per week in research and may or may not have published a single research paper in the last five years. He had not had research support or outside financial assistance during the past five years.

Dental radiology departments ranged in size from 315 to 3,500 square feet. A significant number of schools did not have facilities large enough for small group instruction. Although the majority of schools had separate darkroom facilities for instruction and patient care, a significant number of institutions used a single facility for laboratory and patient care purposes. In two-thirds of the schools surveyed, the radiology department had no responsibility for the maintenance of satellite x-ray facilities.

On the average, there were 1.4 full-time equivalent teachers of dental radiology for schools having 100 students in a class and 0.70 full-time teachers in schools having 50 students per class. One school had one person who devoted 5% of his total professional time to teaching 123 students while at the opposite extreme, another school had three people teaching dental radiology approximately 80% of their time to 50 students per class with a substantial portion of the time being devoted to research and other related activities. This represents a range of 0.0005 to 0.048 full-time equivalent staff to student ratio compared to a minimum ratio of 0.028 recommended by the oral radiology section of the American Association of Dental Schools. Only four schools in the United States met the recommended staffing levels at the time of this survey. Most schools had ratios lower than 0.02 with the majority of schools having fewer full-time equivalent instructors for 100 students.

The BRH supported study also indicated that undergraduate curriculum time ranged from 26 to 288 hours. Lecture time varied from 16 to 56 hours and clinical experience from 13 to 170 hours. There was no clear cut definition of the content of lecture or clinical programs.

The more recent survey published in 1977 contained data which was not dramatically different from the earlier study. Most dental schools were found to offer from 10 to 30 clock hours of didactic material in the first or second year of dental school and from 1 to 20 hours later in the curriculum. Few schools reported courses larger than 30 hours in a single block and it was concluded that there were only slight increases in the amount of curriculum time devoted to teaching radiology compared to previous surveys.

X-ray Technology

The relatively small number of practicing dentists and the long lifespan of typical dental x-ray units limit the size of the marketplace open to manufacturers of x-ray equipment. As a result, a situation has developed in which there is a high level of competition for an economically small market. There is little incentive to develop new technologies or to adapt those developed for other disciplines to dental needs. For the most part, competition centers around style and price so that small inexpensive x-ray units are often popular even though they may necessitate greater patient exposures. Only in the last few years has there been serious discussion about the re-design of equipment and the development of new devices for dental radiology. At the present time few innovations have reached the marketplace. There is considerable reason to believe that most manufacturers of x-ray equipment and accessories are concerned about producing safe and effective units but in our system of free enterprise, there may not be sufficient incentives to encourage the development of state-of-the-art devices.

Many devices currently available in today's marketplace including accurate timers, beam-guiding devices and collimators are not used in the typical dental office.

Professional Attitudes

The attitudes of our professional community can be divided into two parts -- those which are expressed at a national level and those which originate with individuals or small groups at the local level. Nationally, there has been strong opposition to the acceptance of radiology as a speciality within the dental profession. Because of this lack of acceptance, radiology does not have the same stature or importance in the policy making bodies of the American Dental Association (ADA) and in the administrative structure of the nation's dental schools. Teaching and decision making is often left to non-professionals or dentists who have no significant level of training in the radiological sciences. A diagnostic tool which has been successfully used in the eyes of the user is maintained in its existing state because there is little understanding of its inadequacies or of the need for improvement.

The existing state of affairs does not appear to be the result of a calculated attempt on the part of the American Dental Association or any other organization to stifle the growth of radiology but may simply reflect the desire of the ADA to limit the number of dental specialties. The ineffectiveness of minority voices in our professional/political system is also a factor. The American Dental Association has advocated high standards for radiographic practices although the evidence suggests that these standards are not routinely implemented. It is not reasonable to expect adherence to meaningful standards unless the reasons for the standards are clearly understood by the population at which they are directed.

At the local level there is an increasing expression of concern for radiation safety coming from individual practitioners and from constituent dental societies. This concern appears to be based on consumer pressure rather than on familiarity with the radiobiological literature. In the State of Connecticut, state and local societies and members of the State Dental Commission have supported high standards but do not have the resources required for continuing education and monitoring.

Summary and Recommendations

In the last two decades a number of suggestions have been made for reducing exposure to diagnostic x-rays. Many of the recommendations have been incorporated into the performance standards promulgated by the Food and Drug Administration. Other actions which appear to be necessary include: (1) the establishment of minimal educational requirements for those who prescribe x-ray examinations as well as for those who operate x-ray equipment; (2) the development of quality assurance programs which can be carried out in dental offices on a routine basis; (3) a requirement for recording the reason for each x-ray examination, the individual prescribing the examination, the individual operating the x-ray machine, the technique used for the examination, and an estimate of the exposure administered; (4) the periodic inspection and calibration of x-ray generators; (5) the use of beam guiding devices and collimators; and (6) required continuing education.

Mr. ROGERS. Thank you very much, Dr. Reiskin.

There is another call to the floor. I think, if it is agreeable with the members, we will stop at this point and recess for 10 minutes.

[Brief recess.]

Mr. ROGERS. The subcommittee will come to order, please.

Our next witness will be Dr. Rosalie Bertell, Buffalo, N.Y.

Dr. Bertell.

STATEMENT OF ROSALIE BERTELL, PH. D., GNSH

Dr. BERTELL. Thank you, Mr. Chairman.

First of all, I would like to express my gratitude to you and to the committee for all that you have done relative to drawing attention to the low level radiation hazard. There are many of us who appreciate what this committee has done.

Mr. ROGERS. Thank you, Doctor.

Dr. BERTELL. I would like to address the question which is usually skirted, and that is: Exactly what does happen to people when they are exposed to ionizing radiation? I have been rather wordy in my written testimony, [see p. 80] because it isn't easy to get this information, and I will try not to repeat what other people have said, but to go through the kinds of charts that I have provided in the text and explain them to you.

Mr. ROGERS. Excellent.

Dr. BERTELL. My research is based on the Tri-State leukemia survey which was collected between 1959 and 1961 in New York State, Maryland and Minnesota. The population base for the study was 13 million people, and they were surveyed over 3 years. Every leukemia case was picked up and a random sample of controls from this population. Any reports of medical X-ray were verified at the hospital or by the physician, and there are signed reports as to how many plates were taken, what the site was and so on.

To be brief, I will skip to page 5 of the testimony. It is the basic table of the rads which are used in this analysis. I got this from the Department of Health, Education, and Welfare published amounts. You might question the chest X-rays, which looks high. But in the Tri-State, unfortunately, they only made four computer punches; so chest X-ray included thoracic spine, and there were 10 percent thoracic spine and 90 percent ordinary chest X-ray. So that is a weighted average.

The same thing with extremities; they included head, neck, arms and legs. That is also the weighted average.

These are the basic rad doses we used because of the computer punch. What I would like to highlight in the testimony is, that I think the difficulties which are arising with respect to all the environmental diseases, not just the radiation related diseases, stem from two things. One is an inadequate way of measuring the hazard, and the second is poor quality data, so that what I would like to address first is some way to measure hazards that are different from the ways that you are used to seeing.

I would say it is necessary to measure radiation differently because it has such broad effects. When you are dealing with mercury poison and Minamata disease, you have a very specific result of exposure to a hazard; or if you are dealing with lead poisoning or kepone or something. With radiation, the hazards are broad. What has happened is we have focused on how many leukemia cases are expected, forgetting about all the other kinds of degenerative, chronic diseases that are caused.

From my background in math, I know that no matter how many times you wave your hand and say there are very broad based effects to a hazard, if it doesn't occur in your mathematics, then the decisions are not going to be based on this hand waving that says there are a lot of other effects.

The best yardstick which I can find to measure radiation hazard against is the yardstick of natural aging. And in the aging process the fine structure of the cells begin to break down. You don't feel it, but eventually if you live long enough, you realize that something has happened over time. It is the regulatory mechanisms in the body that seem to be affected by radiation, and that is the same kind of thing that happens with aging. So what I did is set out to estimate what happens from radiation when I used as a yardstick what happens in natural aging.

Page 7 is the estimate. In all, I did over 125 separate analyses of the total data in the Tri-State, over 3,000 cases and controls. This represents 20 separate analyses of the total data. Each line is just the result of one analysis, and what I set out to do was to find out at what point it made no difference at all whether the leukemia rate was coming from natural aging or from radiation. So using a fraction having in the numerator the incidence rate due to the radiation; and in the denominator the incidence rate due to the natural aging, the column of adjusted relative risks tell you what the value of that fraction was.

Then in the first column on the left you can see how many years of aging I proposed for each rad. Individual cases and every individual control was evaluated for the amount of radiation, verified diagnostic X-ray they had and then each one was individually evaluated for each different possible aging amount per rad.

It is very remarkable that this type of analysis gives the same results for male and female. This is very unusual in radiation data. It is because I am measuring something different here. I think you will see later that this is important.

Leukemia occurs less frequently in women than in men, and we are not quite sure why. But the radiation effect seems to be the same. That is another reason why I think it is a better way to measure it.

If you notice, what I am getting here is primarily an effect of dental X-ray, because I used a 15 rad cutoff and because the majority of the radiation that was reported in the Tri-State survey was dental. This particular chart is very heavy on the dental X-ray exposure.

In the first line, no estimate of aging was made; and that is a standard analyses showing about a 35 percent or 32 percent, for the female, increase in leukemia due to more than 15 rads of diagnostic X-ray, including dental, and that is significant on the 1-percent level for both males and females.

As you assume the radiation is five one-hundredths of a year aging, you get the second line, the risk comes down; and if you notice, it comes down rather regularly. It reaches about one at 25 percent, or a quarter of a year aging. As you move further down you are getting less leukemia from the X-ray than you are getting from natural aging. Leukemia rate goes up with age, so you are getting less from the X-ray and the fraction gets below one. It gets out of focus when you get down to six-tenths. So it is significant above and below the lines, not within.

I will say, too, in this analysis this not only occurred when the summation risks were taken, but it also occurred within the individual age groups. It was happening across the board.

On the next chart, which is on page 9, I looked only at the trunk X-ray exposures. This was actually the one I did first, and it surprised me. This was only on the males. For the trunk X-ray I used a 5 rad cutoff, so I was getting primarily chest X-rays. And you can see what happens here; it does the same thing. It is the same pattern, and it goes down to about six-tenths of a year aging. And that is primarily chest X-ray effect.

On page 10, you can see the summation of all analyses. There were, in all, 125 separate analyses. The last two I didn't provide the charts for, but when you got over 10 rads and over 15 rads and you limited it to trunk X-ray, you were picking up the GI series, the pelvic examinations, the spinal examinations and so on. These were the heavy abdominal X-rays. So what you have here is a difference in site, difference in the aging effect, depending on whether or not you are hitting the major hemopoietic organs.

I also did some other type of analysis on the same data. If you look at page 13, I introduced a concept of trunk equivalent X-rays, and using what I had found before, that the peripheral dental and arms and legs were about a quarter of a year and trunk was about 1 year, I used a ratio here. I counted the dental in and I counted in the limbs, and so on, but at a rate of one-fourth instead of one. So zero to 10, trunk equivalent X-rays, I calculated by using the controls to estimate the size of the base population that would have been expected to be in that category of trunk equivalent X-ray and what the leukemia rate was per hundred thousand persons. You can see the increase there with the increase of trunk equivalent X-ray. It is rather obvious and the confidence interval there is dependent upon the probability estimate, since you are using a controlled sample to estimate what the whole population would be. Because we had all the cases, we were able to get an accurate estimate of cases. The same thing happens in the over-65-year group.

If you look at the table on page 14, I handled it a little differently here. This was to give you a feeling for what happens in a population as you extend the range of X-ray exposures. These are overlapping categories. In the first line, you are considering only the people who had two or less trunk exposures, and you can see what the leukemia rate is. You might want to compare it with the leukemia rate on the previous page for the same age group which had zero to 10 trunk equivalent X-rays.

This pattern follows all the way through. Leukemia rate goes down right to one X-ray. We are talking about one chest X-ray making a difference in leukemia rate in the population.

If you are trying to control X-rays, you end up controlling range. You try to keep each person under 10 X-rays or under 5 X-rays; so you are really controlling the range.

I think you can see that after a while, even though leukemia rate is still increasing, it is increasing at a slow rate because there are very few people being added to the population at that high rate. So even though you consider a population with the whole range of trunk exposures, if you were talking about low averages, it would give you a leukemia rate of about 2.4. In the previous table you can see that the people who are really getting the X-ray, the high risk group, is getting leukemia at a rate of 5.33. So that average can be deceiving here.

I did this the same way. The previous analysis was for trunk X-ray. The next table is for trunk equivalent. It is the same story. It starts a little bit lower. It still increases as you increase trunk equivalent; that is an important measure.

The same thing for males over 65. The trunk X-rays start at the 6.8 and increase, and the same thing for the trunk equivalent for the men over 65. It is an across-the-board happening.

Mr. **Rogers**. This is the pattern you have found throughout all of your research?

Dr. **Bertell**. That is right. This is a typical pattern.

Mr. ROGERS. So this would apply to all of the X-rays that you have studied?

Dr. BERTELL. That's right.

Mr. ROGERS. Now let me ask you this. What are the highest figures of the incidence of leukemia or cancer or the effect of X-rays with its comparison to aging that you found? And for what types of X-rays?

Dr. BERTELL. I would like to be able to answer that question, and it hinges on the fact that the funding was cut off, and we need to repunch the data. The data has to be repunched. Information is in the folders.

Mr. ROGERS. It simply has to be taken out.

Dr. BERTELL. But it has not been put on computer tape. Therefore, it cannot be analyzed at this point.

Mr. ROGERS. What are the final conclusions that you currently have drawn with your research as to the effect of one X-ray on the human system?

Dr. BERTELL. The best measurement that I can come up with, as far as the leukemia rate increase with the diagnostic X-ray is that one trunk equivalent will raise your risk of leukemia by 4 percent. If your risk is extremely low, you are raising it by a very small amount. But if your risk is high to start with, you are in danger. You are doing something detrimental to the person.

Mr. ROGERS. What about the dental X-ray; do you consider that a trunk X-ray?

Dr. BERTELL. I would say four dental X-rays have the same effect as one trunk X-ray. It is about a ratio of 4 to 1. That is the best number I can come up with, without a repunching of the data.

Mr. ROGERS. Certainly. That is very helpful. I think your studies are certainly what we have been needing. We should finish those so we have some way of evaluating this situation.

Dr. BERTELL. Another big problem is the persons who are already at high risk for leukemia. Dr. Viadana and Dr. Bross published a paper in 1974 showing that if you looked at the medical history of a person, you could find higher susceptibility if they had certain diseases, and they gave these diseases, which I listed on page 19.

My question was: What does radiation do then to the people who were known to be at high risk for leukemia? Table 9 is from the Viadana-Bross paper. It shows that, for the myeloid leukemias, it is a male problem and seems to concern disease group B, which is the pneumonia, heart and rheumatism group.

When I looked at more than 15 rads skin dose diagnostic X-ray for these people—that is on page 20—I found it significantly increased for the males and for the people with disease.

Then I tried something that is new. I tried to combine age and X-ray by using what I call exposure age. Exposure age is whatever your chronological age is plus your trunk X-ray rads and one-fourth nontrunk X-ray rads, and I compared on that instead of comparing just on chronological age.

Mr. ROGERS. What are the results of your comparison, basically?

Dr. BERTELL. That is on page 21. I think the most important thing there is the younger group of men under exposure age 55; you have between 70 and 80 percent of the myeloid leukemia cases coming from that combination. The deaths of those men is hastened by the radiation exposure. Unfortunately, those diseases are often the very diseases that you X-ray for, like heart disease.

It also shows the usefulness of this new measure. What I am picking up there is a risk of 12 for the people in exposure age 35 to 44. That is a very high risk. That is 12 times the normal risk. These men should not be hired in the nuclear industry; they should not work with radiation-related materials.

Mr. **Rogers**. To you, what has been the most startling of your research findings? That figure?

Dr. **Bertell**. I think that is one. I think the heart disease also, which is on 23.

This goes back to what I said before. The state of the person and their basic risk of leukemia is important, and how much that risk is raised by future exposure to radiation. If you have a big risk to start with, then your percentage of that risk is a greater rise in the risk number.

[Testimony resumes on p. 153.]

[Dr. Bertell's prepared statement and attachment follow:]

MEASURABLE HEALTH EFFECTS OF DIAGNOSTIC X-RAY EXPOSURE

Testimony before the Sub-committee
on Health and the Environment, U.S.
House of Representatives, July 11, 1978

This investigation was partially supported by Grant Number CA 11531, awarded by the National Cancer Institute, DHEW.

Rosalie Bertell, PhD,GNSH
151 East Street
Buffalo, NY 14207

BEST COPY AVAILABLE

Introduction:

The living human being is a fantastically complex and delicately balanced organism. It is capable of surviving in many different environments, since it can regulate its inner temperature, acid-base balance, vascular pressure, level of blood chemicals, hormone production, etc. Through these and other regulatory modifications, the human body can cope with the wide variety of foods, pollutants, physical exercise, and emotion, we inflict upon it. This characteristic, so important to normal living, may be called resiliency. Wonderful as it is, however, it does not indicate that we are invulnerable and can survive any bodily insult. Realistic awareness of the limits of resiliency are necessary for continued survival of both the individual and of the race. Transcending these limits overloads the coping mechanisms, causing debilitating chronic diseases and ultimately, death.

One of today's most prevalent body insults, threatening its basic ability to cope, is ionizing radiation. Ironically, it is in the pursuit of health that we subject the body most deliberately to X-ray. We are also exposed to ionizing radiation through proliferation of nuclear weapons and generators, through home fire detectors, from TV and video-terminals, and many other products of the growing industrial and commercial uses of this hazard.

While I will testify today primarily to the hazards of diagnostic X-ray, these other sources of exposure and their cummulative effect on public health is not to be under-estimated. No credible public health stance can condone general exposure to the public for nebulous benefits, while condemning it for the individual seeking medical help. Where appropriate, I will take the liberty of broadening my remarks to include the whole range of ionizing radiation exposures.

For the past nine years I have been studying the environmental causes of leukemia, as indicated by the adult portion of the Tri-State Leukemia Survey. This survey included all leukemia which occurred between 1959 and 1961, in New York State (outside of New York city), Maryland and Minnesota, together with a random sample of the non-leukemic population. The adult portion of the Survey covers 39 million person years, and consists of detailed information on 2800 cases and controls. It is internationally recognized for its excellence.

Further detailed information on the Survey is contained in Appendix I.

It is obvious from the Tri-State data that exposure to medical X-ray is the most important environmental cause of leukemia studied in this survey. There is measurable aging, i.e., break-down of the body's ability to resist leukemia, resulting from routine, so-called harmless, levels of exposure. Medical diagnostic X-rays result in bone marrow exposures between 1 and 168 rad (1), a level permitted to both workers and the general public under Nuclear Regulatory Commission guidelines. While these guidelines do not apply to medical use of

BEST COPY AVAILABLE

X-ray, the results which I am reporting apply also to standards.

In my analysis of the Tri-State Data I am doing several things which are new. The most important methodological change, is that I am measuring the effect of exposure to ionizing radiation against the familiar yard-stick of natural aging. Exposure to low level radiation is imperceptible, as is aging, but both have cumulative effects which eventually become apparent even to the healthiest among us. All of the X-ray considered in this analysis occurred at least one year prior to the leukemia diagnosis for cases, or prior to interview for controls, hence it is the non-repaired cumulative damage caused by this exposure which is being measured.

A word of caution to the biomathematicians who may be present, is in order. The aging effect measured in my research is *not* the same as the "life shortening" effect usually used to assess a hazard. Further discussion of this is in the appendix.

Only X-ray reports verified by the laboratory, doctor or hospital records is included in this analysis. In the Appendix I, details of this verification, and evidence that it does not bias the findings are given.

Mathematical details will be relegated to Appendices, and the main body of the testimony will contain the findings only. Since my findings are at times contrary to some of the assumptions currently accepted in the radiological health field, I will point out where I differ, and the evidence which supports my conclusion.

Mathematical techniques which I am using are the standard techniques, put together in a new way. These techniques were

BEST COPY AVAILABLE

submitted to peer review at the International Biometric Meeting, August 23, 1976. To my knowledge there has been no serious criticism of this methodology. The findings on the aging effect of exposure was presented at the November 1975 national meeting of the American Public Health Association, and is published in the August 1977 issue of the Journal of Surgical Oncology. Additional new findings which I am reporting today follow the same analytic technique, and extend the findings.

Health Effects of Ionizing Radiation:

Measured against the yardstick of human experience with natural aging, affects of exposure to diagnostic X-ray vary with the target area. X-ray of the abdominal cavity or spine is most serious, followed by chest X-ray, and finally by the dental and other non-trunk X-ray. This probably reflects the proportion of bone marrow irradiated, and the exposure of other major organs of the hemopoietic system.

The conversion factors used to change number of verified diagnostic X-ray exposures into the rad skin dose were taken from published values, appropriate to the time of the survey, from the U. S. Department of Health, Education and Welfare. (2) These conversion factors are given in Table 1

Table 1.

Number of milliroentgens used in calculation of skin dose for cases and control, based on: Population Exposure to Xrays, U.S. 1964, U.S. Dept. of Health, Education and Welfare

Site of X-ray	mrad per film (at skin entrance)
Dental	1,138
Chest	167
Abdomen	790
Extremities (includes head and neck)	182

The corresponding bone marrow doses for diagnostic X-ray procedures are given in the Appendix. For dental X-ray, this dose is 1.1 to 3.4 mrad, while for other medical procedures it varies from 3.9 mrad for a chest X-ray to 167 mrad for a spinal X-ray.

Using the skin dose given in Table 1, I calculated the amount of verified exposure in rads for each case and control. Table 2 gives the results of twenty separate analyses of the entire sample. The results of all of these separate analyses, placed in sequential order, reveal the aging pattern which I am trying to clarify. The first line of the table shows the relative risk of exposure to more than 15 rad diagnostic X-ray, when no aging effect is assumed. Relative risk may be thought of as the result of dividing the incidence rate of leukemia among those persons in the population having more than 15 rad exposure, by the incidence rate for those having less than 15 rad exposure. Rates for both males and females are about 34% higher in the exposed group when age adjustment is made. This result is significant on the 5% level.

On line two, the results of a second analysis of the entire sample are given. This time the age of each case and each control was increased by 0.05 times the rad X-ray exposure they had received. The same process is followed and reported for each new estimate of the aging due to X-ray. The object of this tedious process is to find the value for which the relative risk of X-ray exposure becomes one, i.e. incidence rate of leukemia due to radiation exposure is equal to incidence rate due to natural aging.

Table 2.
Tri-State Leukemia Survey

Aging Estimate of Diagnostic X-ray to all Sites incl.Dental

Relative Risks of Non-lymphatic Leukemia with Exposure of 15 or more rad, adjusted for exposure age intervals: 15-44, 45-54, 55-64, 65-74, 75+

# Years Aging per one rad expo.	Age Adj. Rel. Risks		Age and Sex adj. risk	Probability
	Male	Female		
0.00	1.35	1.32	1.34	.0021
0.05	1.27	1.27	1.27	.0136
0.10	1.21	1.16	1.19	.0724
0.15	1.10	1.11	1.11	.2893
0.20	1.05	1.07	1.06	.5333
0.25*	0.98	0.98	0.98	.8333
0.35	0.92	0.87	0.90	.2543
0.40	0.89	0.86	0.88	.1461
0.45	0.89	0.84	0.87	.1199
0.50	0.88	0.83	0.86	.0804
0.55	0.85	0.83	0.84	.0528
0.60	0.86	0.81	0.84	.0457
0.65	0.86	0.81	0.84	.0455
0.70	0.86	0.80	0.83	.0388
0.75	0.85	0.79	0.83	.0294
0.80	0.84	0.78	0.82	.0190
0.85	0.84	0.76	0.81	.0121
0.90	0.85	0.76	0.81	.0135
0.95	0.87	0.76	0.82	.0205
1.00	0.84	0.76	0.80	.0094

N.B. In this Table each of the 450 cases and 824 controls were separately evaluated for rads exposure, and age adjustment.

This treatment of the data makes several things clear. There is a systematic reduction in relative risk, remarkably similar for both males and females, with gradual increase in aging estimate. This reduction approximates one, i.e. the point at which incidence rate from radiation is the same as that from natural aging, when each rad is assigned 0.25 yrs. aging. Since all radiation exposures, including dental were included in this analysis, this effect can be understood as an untargetted, primarily dental X-ray, aging effect.

Another unusual finding is that at this level of analysis there is no difference between the male and female.

Previous analysis limited to trunk X-ray, and to males, showed an aging effect of one rad equivalent to 0.60 yrs. aging for chest X-ray, and one rad equivalent to one year when the target was abdominal. For completeness, the analysis of trunk X-ray which was primarily in the chest area, and the summary aging estimates for all analyses, are given in Tables 3 and Figure 1. These results were published in the Journal of Surgical Oncology, August 1977.

For the remainder of this testimony, I will use the term "exposure age" to mean, for each case and each control, the sum of three terms: chronological age plus number of trunk rads exposure plus one fourth the number of rads nontrunk exposure.

I will now show some of the characteristics of leukemia risk within limited age and sex groups, and secondly, some of the other illnesses related to this aging effect of radiation.

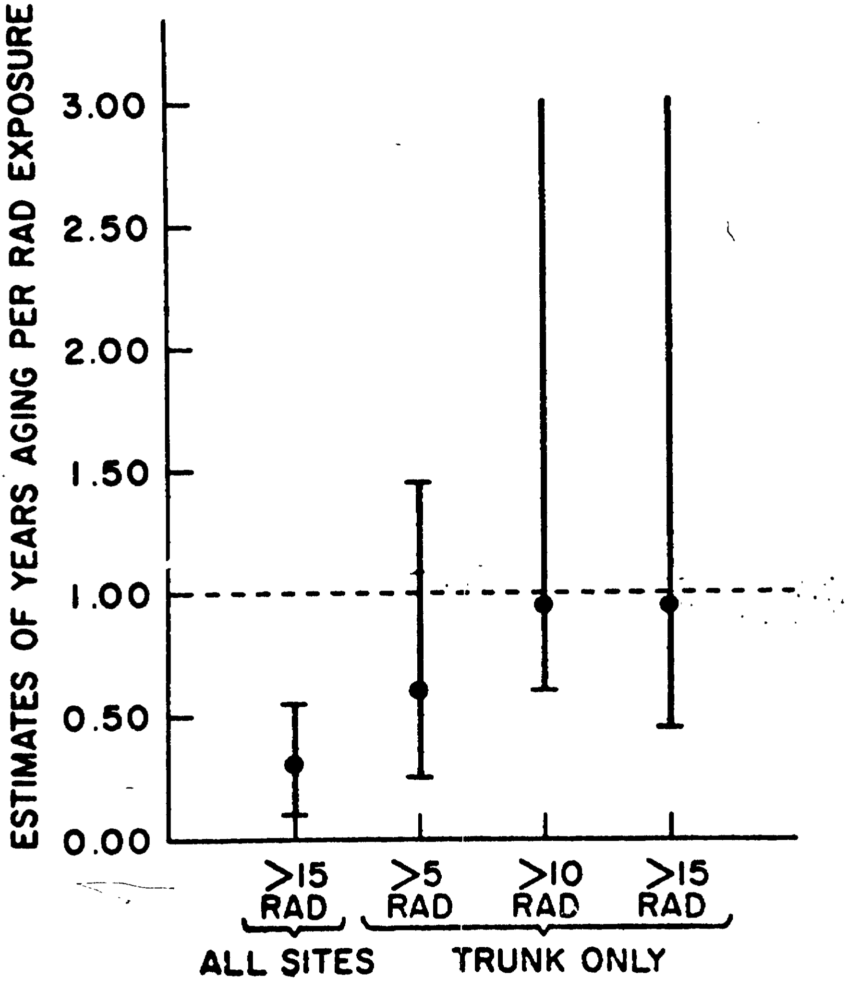
BEST COPY AVAILABLE

Table 3.

Relative Risks of Non-lymphatic Leukemia for Males
Over 45 Years of Exposure Age
with Trunk X-ray Exposure of 5 or More Rads

# Years Aging Per one rad expo.	Age Adj. Rel. Risks	Probability
0.00	1.57	.0017
0.05	1.56	.0022
0.10	1.51	.0036
0.15	1.44	.0101
0.20	1.36	.0295
0.25	1.31	.0522
0.30	1.23	.1220
0.35	1.21	.1558
0.40	1.16	.2706
0.45	1.06	.6489
0.50	1.03	.7952
0.55	1.03	.7718
*0.60	1.00	.9797
0.65	0.99	.8869
0.70	0.94	.5978
0.75	0.93	.5253
0.80	0.92	.4436
0.85	0.90	.3839
0.90	0.94	.5678
0.95	0.92	.4392
1.00	0.93	.5078
1.05	0.91	.4003
1.10	0.89	.3138
1.15	0.90	.3348
1.20	0.88	.2145
1.25	0.87	.2009
1.30	0.86	.1787
1.35	0.85	.1325
1.40	0.84	.1138
1.45	0.82	.0513
1.50	0.79	.0323
1.75	0.76	.0071
2.00	0.74	.0020
2.25	0.71	.0004

Figure 1.


ESTIMATES OF YEARS AGING PER RAD EXPOSURE
3.00
2.50
2.00
1.50
1.00
0.50
0.00
>15 RAD
>5 RAD
>10 RAD
>15 RAD
ALL SITES
TRUNK ONLY

Some Intuitive Sense of the Tri-State Data:

Frequently mathematical presentations of research findings are so "elegant", that the ordinary reader has the feeling that the effect exists only in the mathematics and not in the real world. For this reason, I am including some easily understood tables whichshow that the health effects of medical X-ray are very real, they occur at each level of exposure, and they do not seem to decrease with age.

The male population for the three States surveyed included 2,025,692 between 45 and 64 years of age, and 814,232 over 65, according to the 1960 census figures (3). Based on the proportion of controls for whom verified X-ray reports were obtainable, it would be expected that 1,289,691 males 45 to 64 years, and 466,986 males over 65 years would have verified reports. The male leukemia cases with verified X-ray reports came from this sub-population, and it is possible to estimate the incidence rate of non-lymphatic leukemia per 100,000 within this group. The appendix deals with the question of whether or not the X-ray verification process caused bias in the findings. If anything, it under-estimated the leukemia incidence rate and made the findings conservative. Regardless of this technical aspect of the analysis, it should be obvious from direct examination of these incidence rates that the increase in leukemia is gradual. It cannot be said that a few individuals with large exposure doses cause the effect. By gradually increasing the range of exposures in the population, the rate increases. One can conclude that by controling the range of exposures, the leukemia rate could be lowered.

It is also evident from the data that men over 65 years of age are at least as sensitive to radiation damage as are the men between 45 and 64 years. This is direct evidence which refutes the testimony of Dr. Reginald Gotchy, made as recently as May 24, 1978. Dr. Gotchy is a senior radiobiologist with the Radiological Assessment Branch of the Nuclear Regulatory Commission. To quote his testimony (4):

> "In addition, risk estimates generally decline as age increases (simply an expression of the generalization that the young are more sensitive to the effects of radiation than the old)."

Such casual, untrue assumptions are seriously misleading both to the general public and to the medical profession which has come to rely on the NRC for its information on the health effects of ionizing radiation.

Tables 5 and 7 examine truncated populations for the effect of increased range of trunk exposure. Tables 6 and 8 do the same for trunk equivalent exposure (trunk plus 1/4 non-trunk).

These tables are for visual comprehension and not for dose response curves. They are unsuited for calculating such curves, or for any standard statistical tests which require independent estimates of incidence rates. By comparing the incidence rates in Tables 5 through 8 with the incidence rates within the population actually receiving the increased X-ray, Table 4, one can easily see how averaging masks the true impact. The increased leukemia occurs within the increased exposure group, and the same population average, achieved with a shorter range of exposures, could be expected to decrease total incidence rate.

BEST COPY AVAILABLE

Table 4.
Male Non-lymphatic Leukemia Rates per 100,000 Population

Age	# Trunk equi. Xray*	Lkm. Rate per 100,000/yr.	95% confidence interval for rate
45-64	0-10	1.97	1.80- 2.17
	10-20	2.54	1.93- 3.76
	20-30	3.64	2.45- 7.11
	30	5.33	3.45-11.59
65	0-10	6.91	6.02- 8.11
	10-20	8.51	5.99-14.68
	21-30	20.59	10.73-486.67
	30	24.55	11.54- infinity

* Trunk equivalent Xray means the number of trunk Xray plates plus one fourth the number of dental and other non-trunk Xray plates verified.

NOTE: THIS TABLE CANNOT BE USED TO ESTIMATE DOSE RESPONSE BECAUSE AVERAGE DOSE AND AVERAGE AGE IN THE SUB-CATEGORIES IS NOT GIVEN.

Table 5.

Tri-State Leukemia Survey
Non-Lymphatic Leukemia Rates by X-ray Exposure for Males 45-64 Years of Age

Range trunk exposures *	# Cases	Lkm. rate per 100,000/yr.
0- 2	30	1.59
0- 5	40	1.63
0-10	58	1.99
0-15	65	2.04
0-20	74	2.14
0-25	81	2.26
0-30	82	2.24
0-40	84	2.21
0-50	89	2.32
0-70	91	2.376
0-80	92	2.378
0-120	93	2.404

* Number of X-ray plates used for chest or abdominal or other trunk X-ray.

NOTE: THIS TABLE CANNOT BE USED FOR A DOSE RESPONSE ESTIMATE BECAUSE DOSE IS GIVEN IN OVERLAPPING RANGES. AVERAGE DOSE FOR EACH RANGE, AND AVERAGE AGE FOR EACH RANGE ARE NOT GIVEN.

Table 6.

Tri-State Leukemia Survey
Non-Lymphatic Leukemia Rates by X-ray Exposure
for Males 45-64 Years of Age

Range trunk equiv. expo.*	# Cases	Lkm. Rate per 100,000/ yr.
0- 2	17	1.34
0- 5	34	1.79
0-10	53	1.97
0-15	63	2.03
0-20	69	2.08
0-25	77	2.20
0-30	80	2.21
0-40	84	2.22
0-50	88	2.23
0-60	90	2.35
0-70	91	2.376
0-80	92	2.378
0-120	93	2.404

* Trunk equivalent exposures includes each actual trunk exposure plus one fourth the number of non-trunk exposures (dental, and extremity)

NOTE: THIS TABLE CANNOT BE USED FOR A DOSE RESPONSE ESTIMATE BECAUSE DOSE IS GIVEN IN OVERLAPPING RANGES. AVERAGE DOSE FOR EACH RANGE, AND AVERAGE AGE FOR EACH RANGE ARE NOT GIVEN.

Table 7.

Tri-State Leukemia Survey
Non-lymphatic Leukemia Rates by X-ray Exposure for Males 65 or more years of age

Range trunk exposure *	# Cases	Lkm. Rate per 100,000/yr.
0- 10	72	6.80
0- 15	87	7.23
0- 20	99	7.55
0- 25	107	8.05
0- 30	108	8.01
0- 40	110	7.85
0- 50	114	8.14
0- 60	116	8.28
0- 70	118	8.42
0- 80	119	8.49
0-100	121	8.64

* Trunk exposures include all X-ray plates verified for trunk.

NOTE: THIS TABLE CANNOT BE USED FOR A DOSE RESPONSE ESTIMATE BECAUSE DOSE IS GIVEN IN OVERLAPPING RANGES. AVERAGE DOSE FOR EACH RANGE, AND AVERAGE AGE FOR EACH RANGE ARE NOT GIVEN.

Table 8.
Tri-State Leukemia Survey
Non-lymphatic Leukemia Rates by X-ray Exposure
for Males 65 of more Years of Age

Range trunk equiv. expo.*	# Cases	Lkm. Rate per 100,000/yr.
0- 10	67	6.91
0- 15	81	6.83
0- 20	93	7.30
0- 25	102	7.78
0- 30	108	8.01
0- 40	110	7.85
0- 50	114	8.14
0- 60	116	8.28
0- 70	118	8.42
0- 80	119	8.49
0-100	120	8.57
0-110	121	8.64

* Trunk equivalent exposures includes the number of trunk X-ray plates and one fourth the number of dental and other non-trunk X-ray plates verified.

NOTE: THIS TABLE CANNOT BE USED FOR A DOSE RESPONSE ESTIMATE BECAUSE DOSE IS GIVEN IN OVERLAPPING RANGES. AVERAGE DOSE FOR EACH RANGE, AND AVERAGE AGE FOR EACH RANGE ARE NOT GIVEN.

Estimating the Public Health Impact of Ionizing Radiation:

In my approach to this question, I have tried to emphasize the need for differential protection. Some persons, such as pregnant women, are at a greater risk than others. I have tried to identify other sub-populations, not so well recognized as needing special protection, who show marked susceptibility to radiation damage. I believe that these persons need special protection both from medical X-ray, and from employment involving exposure to ionizing radiation.

Since differential protection is often impossible in routine X-ray practices, mass screening programs, employment and hospital admission policies, etc., my remarks should be taken as very critical of these mindless uses of radiation. I am also assuming that strict licensing of X-ray technicians, inspections of equipment, reductions of per film exposures, elimination of defensive radiology, taking of X-rays when treatment cannot be improved with improved knowledge, using X-ray equipment in order to make it cost effective, and other abuses will be addressed by others who will be giving testimony today.

Special knowledge gained from study of the Tri-State Data, which is not easily gained from any other source, will be emphasized in my testimony.

BEST COPY AVAILABLE

In an article published in 1974, Dr. Enrico Viadana and Dr. Irwin D.J.Bross identified certain diseases, diagnosed five years or more prior to the diagnosis of leukemia (or interview, for the controls), as indicators of susceptibility to leukemia (5). These diseases probably indicate a break-down in the body regulatory and immuno-systems, leaving the person vulnerable to the disease. In the Viadana analysis, diseases were grouped as follows:

GROUP A: Asthma, hay fever, hives, eczema, goiter, diabetes mellitus, herpes zoster, psoriasis, neurodermititis, TB.

GROUP B: Pneumonia, heart, rheumatism.

The selections from Table II, in this publication, which pertain to non-lymphatic leukemia are reproduced here for your convenience.

Table 9.

STATUS	LEUKEMIA TYPE	SEX	REL.RISK	PROBABILITY
One disease from A; one from B	Myeloid	Men	5.55	0.00
	Myeloid	Women	1.95	0.14
One disease from A; none from B	Myeloid	Men	1.72	0.16
	Myeloid	Women	1.43	0.29
One disease from B; none from A	Myeloid	Men	1.80	0.01
	Myeloid	Women	3.38	0.09

The inter-action between disease and X-ray exposure in increasing the risk of non-lymphatic leukemia was not attempted in the Viadana analysis. As a first analysis of this inter-action, I did a standard analysis of the adult sample, matching for age, sex, and disease category. By matching cases with the disease indicators with controls with the disease indicators, any excess of radiation exposure due to the indicator diseases is controlled for in the analysis. I used one year prior to the diagnosis of leukemia, or prior to interview for the cases, as a cut-off point for indicator diseases. No diseases or X-ray occurring after that cut-off was considered. Except for some combinations of allergies, no case or control reported more than one of the diseases in Group A. The diseases in Group B were more common. The Tri-State Data contains detailed information, and a time-line study of disease diagnosis and medical X-ray would be possible if re-coding were undertaken. At the present time such a detailed analysis is impossible.

The preliminary gross overview of the interaction of indicator diseases and X-ray exposure gave the following results:

Table 10.

Relative Risk of Non-lymphatic Leukemia With Exposure to 15 rad or more Skin Dose Diagnostic X-ray for Persons with and without Indicator Diseases

CATEGORY	WEIGHTED OVER	REL. RISK	PROBABILITY
Male	age/disease	1.79	0.00
Female	age/disease	1.09	0.52
With disease	age/sex	1.59	0.00
Without disease	age/sex	1.12	0.44
Summary	age/sex/disease	1.47	0.00

There was strong indication that both disease and X-ray were involved in the male leukemogenesis. I then did a new analysis of the entire sample, using exposure age, i.e. an age adjusted for X-ray exposure (as previously described), instead of chronological age. In this analysis all relative risks were reduced to about one, as was expected. This change to exposure age effectively adjusts for the leukemogenic effect of X-ray, enabling a disease effect to be more directly evaluated. Table 11 shows the results of the analysis of the risk of leukemia for persons having the indicator diseases relative to those not having the indicator diseases, for males. These findings are startling, and of great importance for designing radiation protection programs for public health.

Table 11.

Relative Risk for Nonlymphatic Leukemia
for Males with Indicator Diseases, for Exposure Age

Exposure Age	No.Cases	No. Controls	Rel.Risk	Probability	Attributable Prop.
15-34	15	50	1.34	0.34	14%
35-44	13	22	11.78	0.00	77%
45-54	16	53	7.27	0.00	75%
55-64	40	81	1.15	0.59	8%
65-74	50	63	1.58	0.12	28%
75-84	44	35	1.22	0.56	13%
85 or more	53	36	4.08	0.00	70%
Summary	231	340	1.91	0.00	37%

This is strong evidence that the younger men dying of non-lymphatic leukemia will have had prior indications of medical break-down. These men can be precipitated into a risk category 12 time that of other young men by ionizing radiation. Differential protection of these young men is important. The exact diseases involved could be further determined, but the present evidence is sufficient for precautionary measures to be immediately taken. Young men with the disease indicators listed on page 19 of this testimony, should not have any unnecessary medical X-ray examinations, and should not be employed in industries dealing with radioactive material. Needless to say, indiscriminate increase in background radiation from weapon testing or from the nuclear industry will hasten the death of these young men. They are certainly among the most sensitive to the acceleration of aging due to this exposure.

The inability to identify the combination of disease indicators as indicators of leukemia in the females may be either a real difference or an artifact due to the X-ray verification process. I suspect that it is the latter. As explained in the Appendix, verification tended to exclude female leukemics more than males.

Since heart disease was the most frequent disease among the indicator diseases identified by Viadana, I undertook a separate analysis of the interaction of this disease with X-ray exposure. For this disease, male and female risks were quite different when chronological age was used for matching. The highest risk for males, 2.30, occurred between 45 and 54 years, the period at which the least risk, 0.75, occurred for the female. The highest risk for the female occurred for those over 75 years of age, 2.75, while the corresponding male risk was 0.71. The highest combined male/female risk was 2.02.

After adjustment for exposure age there was a marked similarity in the male and female risks, with the combined risk in the 45 to 54 exposure age category reaching 6.01. Obviously exposure age better identifies the high risk group, and matching on exposure age brings out the male/female similarity in risk very clearly.

Again, exposure to ionizing radiation hastens the onset of leukemia in these high risk people.

Tables 12 and 13 give the results of this analysis.

Table 12.

Risk of Non-lymphatic Leukemia for Persons
With Heart disease Relative to Persons
Without Heart Disease

Chronological Age	Relative Risk Estimate Male	 Female	 Combined
15-44	1.27	1.67	1.45
45-54	2.30**	0.75	1.50
55-64	2.17**	1.77	2.02**
65-74	1.26	1.06	1:17
75 or more	0.71	2.75	1.59
Summary	1.38*	1.50*	1.44**

* Significant on 5% level; ** Significant on 1% level.

Table 13.
Risk of Non-lymphatic Leukemia for Persons
With Heart Disease Relative to Persons
Without Heart Disease

Exposure Age	Relative Risk Estimate Male	Female	Combined
15-44	0.88	1.04	0.95
45-54	6.33**	5.71**	6.01**
55-64	1.33	2.09*	1.58*
65-74	1.01	1.16	1.07
75 or more	1.79*	1.58	1.67**
Summary	1.48*	1.47*	1.47**

* Significant on the 5% level; ** Significant on the 1% level.

From these few examples it should be apparent that the measurement of the aging effect of exposure to ionizing radiation is useful. It certainly clarifies the relationship between disease indicators and non-lymphatic leukemia in those under age 50. The implications of this research for clinical practice and for workers in radiation related industries should be obvious. I would also conclude that monitoring these indicator diseases in a population might be more useful, from a public health point of view, than waiting until one can count deaths from leukemia. Their incidence rates and age of occurrence might be used as an early warning signal of deterioration of the public health.

Quantifying Both Aging and Radiation Effect on Leukemia Rates:

Aging is a rather familiar process for those of us who have lasted beyond age forty. Therefore I have appealed to an intuitive sense of gradual break-down in the body's ability to cope, and thusfar just measured exposure to ionizing radiation against that yardstick. It is possible, however, to go further, and quantify that breakdown in terms of incidence rate of leukemia. In the appendix of my published paper: "X-ray Exposure and Premature Aging", I have discussed this problem in detail. I will include that paper with my testimony.(~~5~~6)

The conclusion that I have reached is that the aging process in the U.S. during the time prior to the Tri-State Survey, increased the individual risk of non-lymphatic leukemia at a rate of 5 to 6% a year. This risk accumulates in the same way as does compound interest.

Figures 2, 3 &4 are graphs showing the cumulative relative frequency of each age group in the survey area, based on information in the 1960 census. The shaded band indicates the expected cumulative relative frequency of non-lymphatic leukemia cases under the assumption that incidence rate increases 5 to 6% a year, compounded. Figures 2 and 3 give male and female results separately. Figure 4 gives the combined cumulative frequencies. By using this method of relative frequency, difference between male and female absolute incidence rates are blurred, and the commonality of the selection process highlighted.

Figure 2.

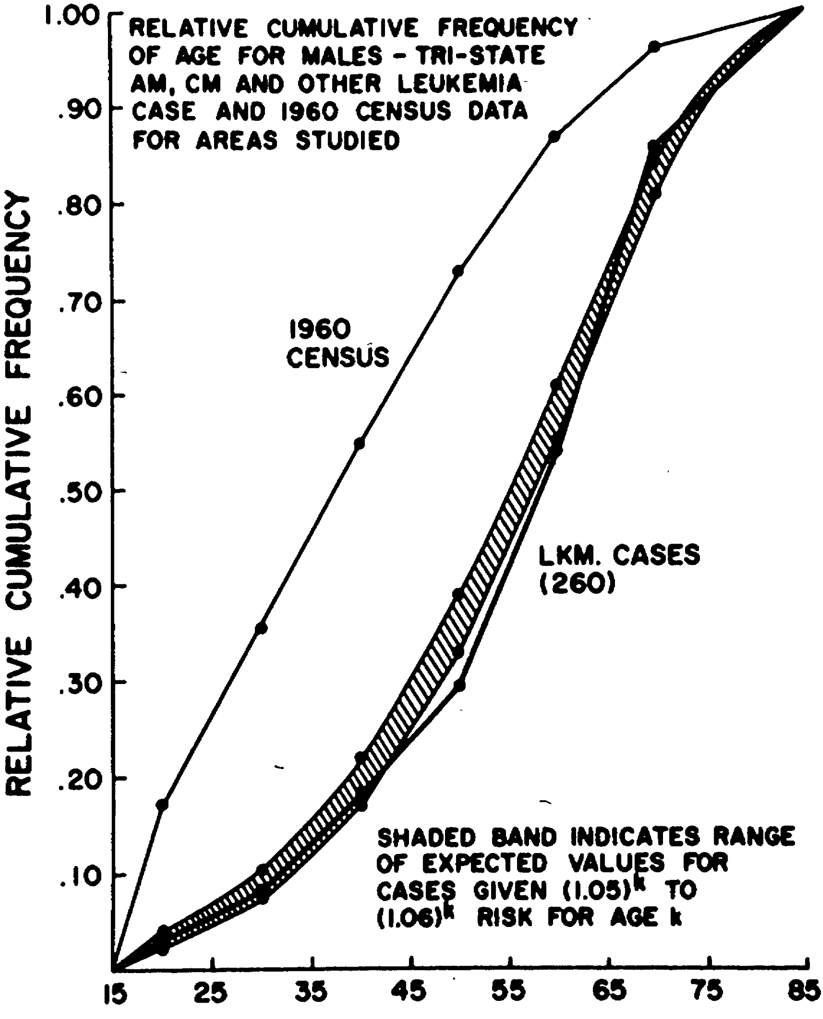

RELATIVE CUMULATIVE FREQUENCY OF AGE FOR MALES - TRI-STATE AM, CM AND OTHER LEUKEMIA CASE AND 1960 CENSUS DATA FOR AREAS STUDIED
1960 CENSUS
LKM. CASES (260)
SHADED BAND INDICATES RANGE OF EXPECTED VALUES FOR CASES GIVEN (1.05)^k TO (1.06)^k RISK FOR AGE k
RELATIVE CUMULATIVE FREQUENCY
1.00
.90
.80
.70
.60
.50
.40
.30
.20
.10
15
25
35
45
55
65
75
85
AGE IN YEARS

Figure 3.

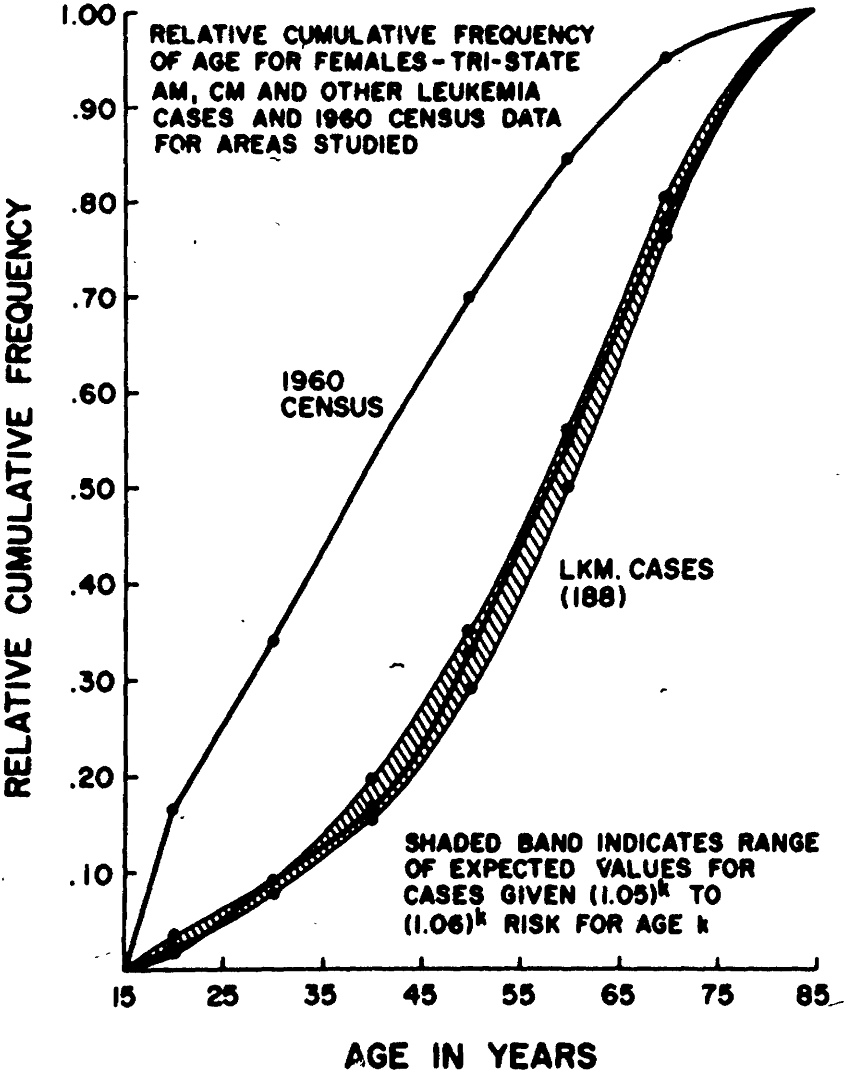
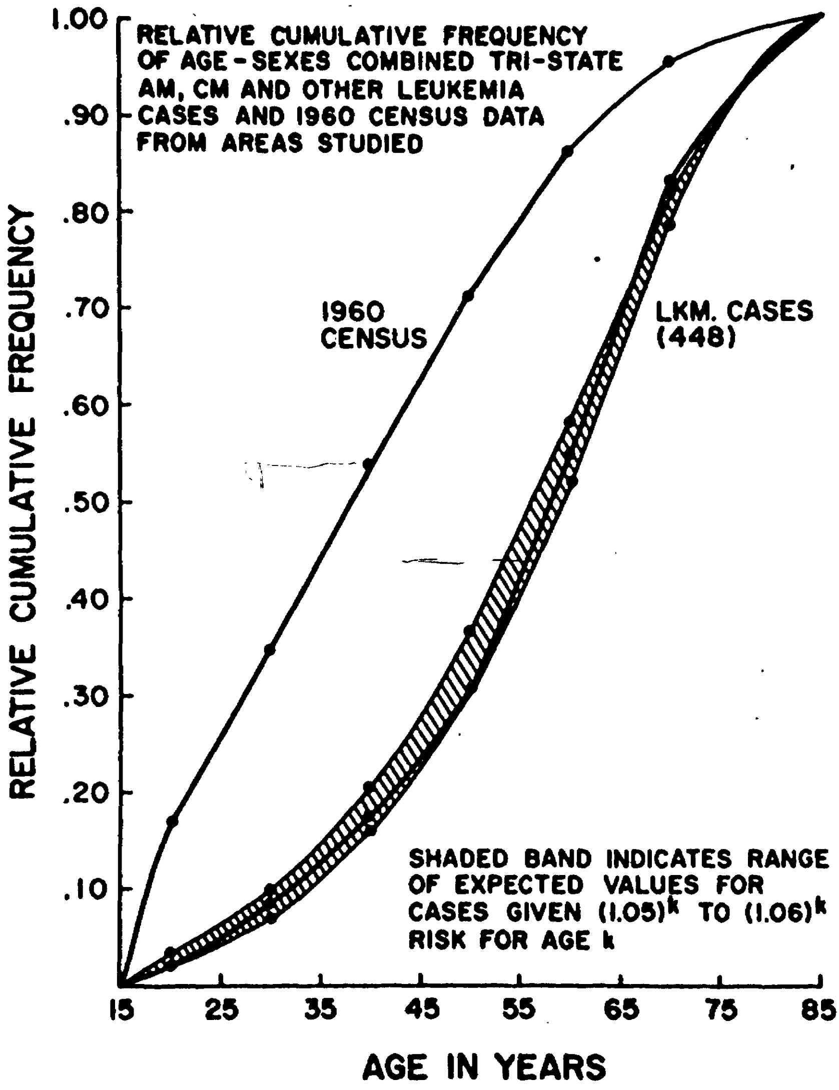

RELATIVE CUMULATIVE FREQUENCY OF AGE FOR FEMALES - TRI-STATE AM, CM AND OTHER LEUKEMIA CASES AND 1960 CENSUS DATA FOR AREAS STUDIED
1960 CENSUS
LKM. CASES (188)
SHADED BAND INDICATES RANGE OF EXPECTED VALUES FOR CASES GIVEN (1.05)k TO (1.06)k RISK FOR AGE k
RELATIVE CUMULATIVE FREQUENCY
1.00
.90
.80
.70
.60
.50
.40
.30
.20
.10
15
25
35
45
55
65
75
85
AGE IN YEARS

Figure 4.

EXAMPLE OF A "COMPOUND INTEREST" MATHEMATICAL MODEL

FOR PREDICTING THE AGE DISTRIBUTION OF THE

LEUKEMIA PATIENTS IN THE TRI-STATE SURVEY



In Figures 2, 3 & 4, only the non-lymphatic leukemia cases with verified X-ray reports were used. The selection rate holds also for the entire sample, and the use of this sub-set was both to show that the verification process had not biased theage selection seriously, and to facilitate direct comparison of aging with verified X-ray exposures.

The next 7 figures show the Tri-State controls and a mathematical model which predicte the cumulative relative frequency of the cases on the assumption that one trunk X-ray increases the risk of non-lymphatic leukemia 5%, compounded. The controls and predicted case curve are the same in all figures. This model is statistically acceptable for each of the three leukemia types and each of the two age groups separately and when combined. There is no other curve which will fit each of these series of cases and age groups separately and when combined.

The "official" estimates of dose response for leukemia with exposure to ionizing radiation are made on a straight line basis, and this does well as an approximation in a short range of exposures. I suspect that the true shape of this curve is sigmoid, and that I am picking up the curve at a much lower dose range where some of the curved portion occurs. The curve which I am observing will form a plateau before reaching the upper range of radiation exposures usually used to estimate. Hence the leukemia rate at this lower dose level is higher than would be predicted by methods used in the BEIR report.

Figure 5.

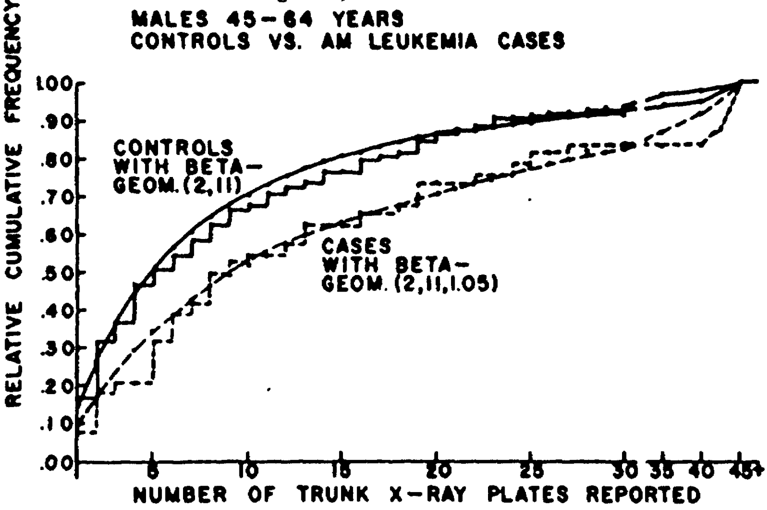


Figure 6.

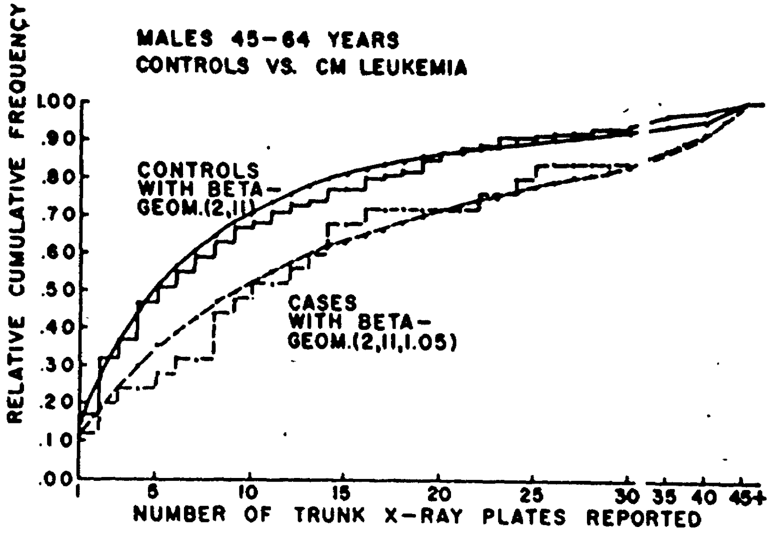


Figure 7.

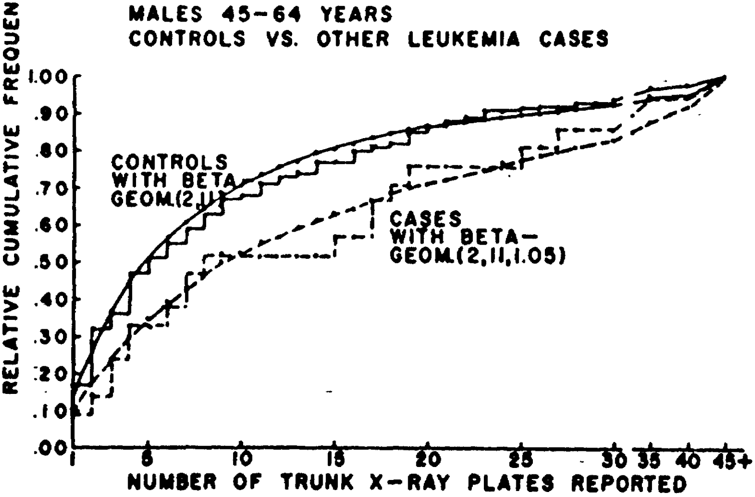


Figure 8.

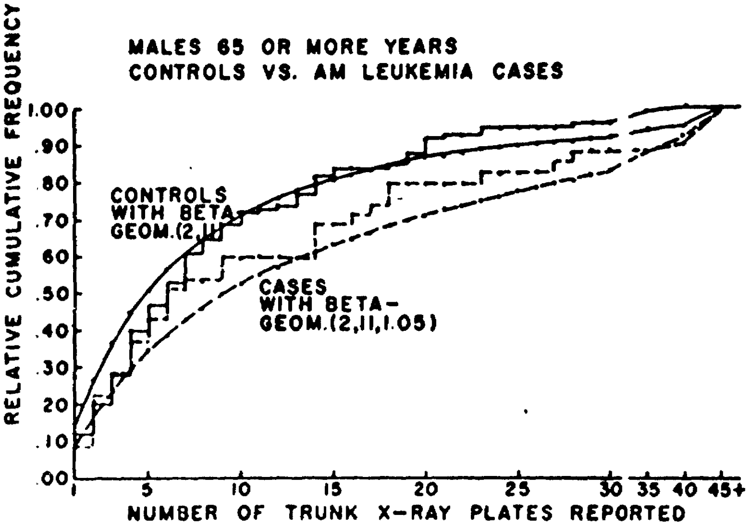


Figure 9.

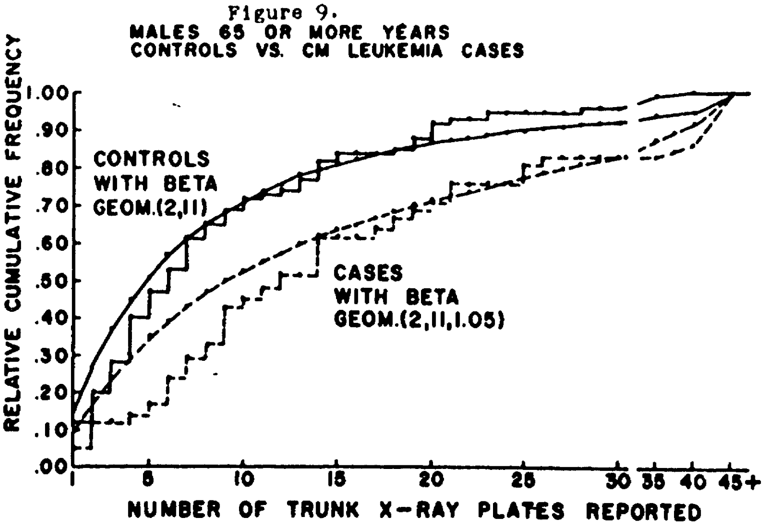


Figure 10.

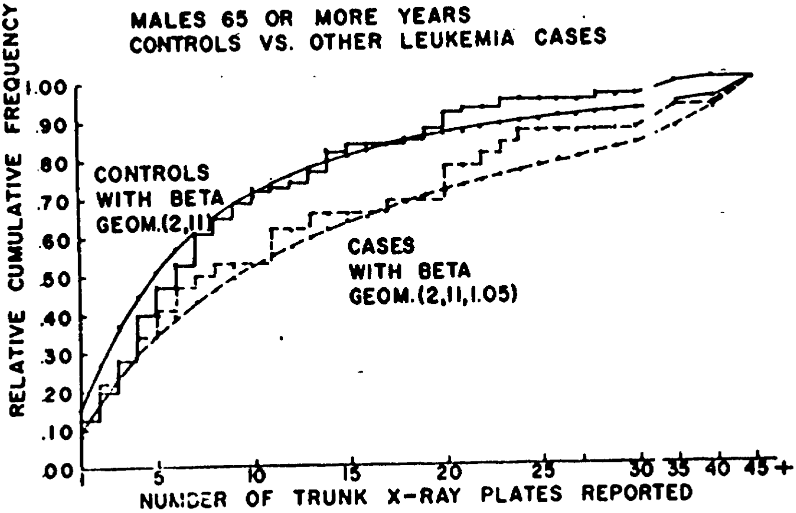
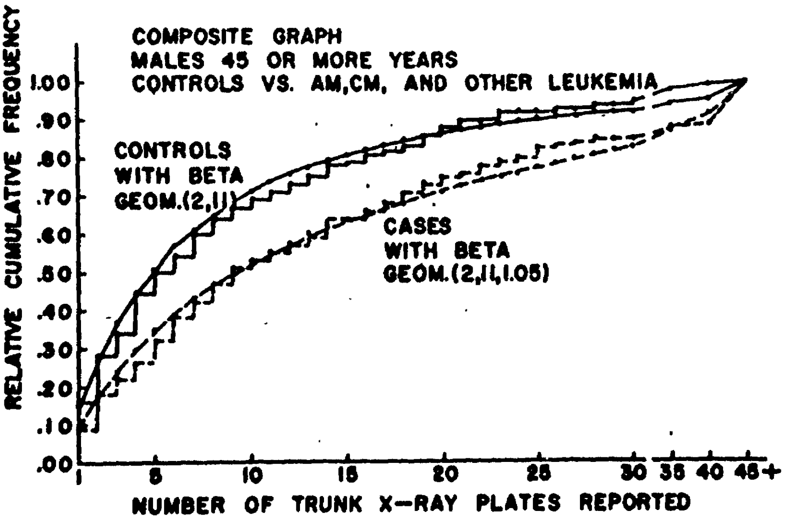


Figure 11.


COMPOSITE GRAPH
MALES 45 OR MORE YEARS
CONTROLS VS. AM, CM, AND OTHER LEUKEMIA
CONTROLS
WITH BETA
GEOM.(2,11)
CASES
WITH BETA
GEOM.(2,11,1.05)
RELATIVE CUMULATIVE FREQUENCY
1.00
.90
.80
.70
.60
.50
.40
.30
.20
.10
.00
1
5
10
15
20
25
30
35
40
45+
NUMBER OF TRUNK X-RAY PLATES REPORTED

Although I have not attempted a rigorous mathematical proof in this testimony, it is not difficult to show that the increase in leukemia risk with X-ray must be both proportional to the risk already accumulated by the individual, and exponential rather than linear. The proportionality of the risk has been amply demonstrated in the sub-population at risk because of disease indicators, and in the estimates for risk increase with trunk X-ray.

With respect to the linear hypothesis, I would make the following observations: First, aging is obviously an exponential process, not a linear process. Second, the most remarkable outcome of the analysis presented in Table 2 of this testimony, indicates that the under-lying mathematical process of radiation induced non-lymphatic leukemia follows the same mathematical process as aging induced disease. Changing the ages of 450 leukemia cases and 824 controls in a systematic way to reflect their individual diagnostic X-ray experience could not bring about such consistent results if the two characteristics, natural aging and radiation exposure, were not interchangeable.

The following Tables give the expected numbers of non-lymphatic leukemia cases for the Tri-State area under the assumption that there is no increase in rate due to X-ray exposure. The Chi Square test allows rejection of this hypothesis. The alternate hypothesis which assumes a 4% increase in risk with each X-ray plate taken is shown to be acceptable under the same Chi-Square test. The tables also give estimates of the number of extra cases which occurred because of the X-ray.

Table 14.

Tri-State Leukemia Data for

Males 45-64 yrs.

# Verified Chest X-ray	# Cases Observed	# Cased Expected (null hypothesis)	# Cases Expected (1.04 risk/plate)
0	28	28	28
1	17	14.45	15.03
2	12	10.02	10.84
3-5	12	11.17	13.06
6-10	13	5.93	8.62
11-20	8	4.44	7.99
21 or more	3	1.22	3.26
SUM	93	75.23	86.80

Chi-square test for the expected number of cases under the null hypothesis: 14.78, with 5 DF, which is significant on 3% level.

Chi-square test for the expected number of cases under the hypothesis of a 1.04 relative risk per plate: 2.72, with 4 DF, not significant.

Note: Cases were taken over a three year period, and the expectations were for the same period of time.

This Table looks at chest X-ray data only. Persons with no verified chest X-ray may have had abdominal or non-trunk X-ray. As a rough estimate of extra leukemia cases in the verified chest X-ray categories for this age group, one could subtract the number expected under the null hypothesis from the actually observed number. There were 17.77 "extra" cases, about 19.1% of the total number observed.

Table 15.

Tri-State Leukemia Data for

Males 65 yrs. or more

# Verified Chest X-ray	# Cases Observed	# Cases Expected (null hypothesis)	# Cases Expected (1.04 risk/plate)
0	29	29	29
1-2	42	38.25	40.57
3-5	21	19.52	22.32
6-10	18	10.59	14.21
11-20	9	3.91	7.04
21 or more	2	1.34	3.56
SUM	121	102.61	116.7

Chi-square test for the expected number of cases under the null hypothesis: 12.62, with 4 DF, which is significant on 3% level.

Chi-square test for the expected number of cases under the hypothesis of a 1.04 relative risk per plate: 2.37, with 3 DF, not significant.

Note: Cases were taken over a three year period, and the expectations were for the same period of time.

This Table looks at verified chest X-ray only, for the males over 65 years of age. There are 18.39 "extra" cases, above the number predicted by the null hypothesis. This is about 15.2% of the total.

The story is essentially the same when one looks at trunk equivalent X-ray instead of chest X-ray. This estimates all of the X-ray verified, using the four to one equivalence for non-trunk X-ray. Tables 16 and 17 present this information.

Table 16.

Tri-State Leukemia Survey Data

Males 45-64 Years

# Trunk Equiv. X-ray	# Cases Observed	# Cases Exp. (null hypothesis)	# Cases Exp. (1.04 risk/plate)
0-10	53	53	53
10+ -20	16	12.42	18.36
20+ -30	11	5.94	13.00
30+	13	4.80	15.54
Sum	93	76.16	99.90

Chi square test for the expected number of cases under the null hypothesis: 19.35, with 2 DF, which is significant on 1% level.

Chi square test for the expected number of cases under hypothesis of a 1.04 relative risk per trunk equivalent: 1.03, with 1 DF, NS

Males 65 or more Yrs.

# Trunk Equiv. Xray	# Cases Observed	# Cases Exp. (null hypothesis)	# Cases Exp. (1.04 risk/plate)
0 -10	67	67	67
10+ -20	26	21.10	31.23
20+ -30	15	5.03	11.03
30+	13	3.68	11.93
Sum	121	96.81	121.19

Chi square test for the expected number of cases under the null hypothesis: 44.50, with 2 DF, significant on 1% level.

Chi square test for the expected number of cases under hypothesis of a 1.04 relative risk per trunk equivalent: 2.40, 1 DF, NS

Note: In the above tables observed and expected numbers are for the three year period.

A realistic public health goal might be to limit each persons X-ray exposure to one half trunk equivalent X-rays per year, on an average. In the Tri-State Survey, 69.6% of the male controls 45 to 64 years, and 69.2% of the male controls over 65 were within this limit. As indicated in Tables 16 and 17, this would prevent 18.1% and 20.0% of the non-lymphatic leukemia cases in these two groups. This means preventing one out of five, or one out of six cases. If this were a cure rate it would be quite remarkable! Concern for prevention should be just as important as concern for cure.

There would obviously be emergency situations which would over-ride the above limit, but I believe that it is workable as a guideline.

Such a limitation would raise consciousness about this hazard, and this is necessary because of all of the public relations material now being circulated, which would claim that exposures of this order of magnitude offer negligible health risk. The medical profession cannot afford to take the guidance of the nuclear industry in a public health issue where they should be assuming the leadership. Limiting medical X-rays, even when there is some benefit to the individual, when the overall risk exceeds the benefit, would put in a new perspective the risks being planned for workers and the general public for nebulous "growth of the economy" reasons. I am also fearful that medical X-ray will become a scapegoat, and needed uses of medical X-ray will be sacrificed because of economic gain hoped for in the use of nuclear power or nuclear weapons. This could become one more way of putting the public health second to economic gain!

Summary and Recommendations:

The main point of my testimony is to convey an important concept. Just as it would be ludicrous to try to convince the general public that growing old is not "harmful" since not every elderly person gets leukemia, so it is also ludicrous to call exposure to ionizing radiation "harmless" in terms of the number of leukemias it might be expected to cause. The mathematics which are used should reflect the general nature of the biological breakdown slowly caused by exposure to low level radiation. I strongly propose that natural aging be used as the yardstick for this measurement. There seems to be no indication that the advisory or regulatory bodies responsible for protecting the public health from radiation are even taking the trouble to investigate this approach.

My second important point is that the gathering of vital statistics information in this country is designed to monitor the public health problems of the past, namely infectious diseases, and is inadequate for monitoring environmentally caused diseases. This is not a lack of knowledge or ability to monitor such diseases. I am enclosing the title page of a recommendation recently made to the National Center for Health Statistics by the U.S. National Committee on Vital and Health Statistics (7). This publication supports my claims, as does the present unfortunate series of disputes over saccharine, mirex, PCB, PBB, kepone, red food dyes, and radiation. If information is properly gathered, all of these environmental hazards can be monitored. It is not necessary to mount a study for each one.

Another source of difficulty with respect to researching environmental hazards is the gowth of defensive science. By this, I mean science specifically designed to prove a commodity or technology "harmless". Such science is often "bought" with the tax payer's money. Science not supportive of a course desired on an economic basis is, on the other hand, penalized in many ways. Scientists should be able to work outside of the rewards and punishments of the "system". They should be able to report their findings, and let the chips fall where they may. This is impossible especially for any radiation related research, since vested interests relative to this hazard encompass the military, the nuclear industry, banks, government agencies, foreign relations, the medical establishment, insurance agencies, the American College of Radiologists, the American Cancer Society, the American Nuclear Society, etc. This has to be the most awsome lobby ever encountered in the history of American politics!

There are more parts to this radiation story, esecially the whole question of radiation damage of germ cells which cause deleterious effects apparent in subsequent generations. I have also not touched on the special sensitivity of the fetus and young child. The effects of ionizing radiation are better known in these areas of research, and Dr. Bross has recently testified before this committee on these aspects. It has been my purpose to provide you with information which you can get from no other source. With a complete lack of financial support even this service is not as complete as it could or should be.

Appendix I - The Tri-State Leukemia Data:

In the main body of my testimony, I have set forth the concept of aging, i.e. breakdown of the body regulatory systems which gradually undermine the individual's ability to cope with life, and measured the biological damage done by ionizing radiation against this yardstick. In the usual biostatistical jargon, there is a term: "life-shortening effect". This is calculated by determining the number of premature deaths expected in a population exposed to some hazard, estimating the number of man years lost by these premature deaths, and then dividing this number of man years lost by the size of the population. Thus if two persons die 30 years prematurely in a population of one million, $30/10^6$, or 0.00003 yr. is "lost" per person. In other words, the two premature deaths can be considered a 16 minute "life-shortening" for the population. What I am talking about has no relation to this myth.

Table 17 gives the population base from the Tri-State region from which the survey information was collected. It also gives the theoretical cumulative relative frequency values expected for the non-lymphatic leukemia cases under the hypothesis that risk increases at a rate of 5%, and 6% per year of natural aging. These numbers are the basis of the banded interval in Figures 2,3 and 4 of this testimony. A mathematical decription of the way these numbers are generated is given in the appendix of my published paper: "X-ray exposure and Premature Aging."

Table 17.

Age distributions based on 1960 census data
for areas involved in Tri-State Leukemia Survey

Age	Number of Persons	Rel. Cum. Freq.	Theoretical Rel. Cum. Freq. Curves for rel. risks $(1.05)^t$ and $(1.06)^t$ for t years beyond 15 T_5	T_6
15-24	2,183,654	16.8	3.6	2.4
25-34	2,301,104	34.5	9.7	7.1
35-44	2,502,232	53.7	20.5	16.0
45-54	2,287,864	71.3	36.7	30.7
55-64	1,869,281	85.7	58.3	52.2
65-74	1,273,975	~~95.5~~	82.2	78.4
75+	583,860	100.0	100.0	100.0
Σ	13,001,970			

Table 18. gives the age distribution of the entire non-lymphatic leukemia sample from the Tri-Sate Survey, regardless of whether or not the cases had verified X-ray exposure reports. The observed cumulative frequencies given, and combinations of the two M-type leukemias, and of all three categories are given. The intuitive sense that combination of these leukemia types on the basis that differences in age patterns are random, and the underlying age-selection process is the same, is tested by a Kolmogorov-Smirnov Test of Homogeneity. The results of these tests are shown in Table 19. Since the non-lymphatic leukemias show comparable deviations from the census distribution, and consistent patterns with one another, they were combined in the analysis.

Table 18.

Age distributions by leukemia type -- Tri State Survey

Age	AM No.	AM Rel. Cum. Freq.	CM No.	CM Rel. Cum. Freq.	OTH No.	OTH Rel. Cum. Freq.	AM and CM No.	AM and CM Rel Cum. Freq.	AM,CM and OTH No.	AM,CM and OTH Rel. Cum. Freq.
15-24	19	5.7	9	3.5	7	3.1	28	4.7	35	4.3
25-34	27	13.8	15	9.3	12	8.5	42	11.9	54	10.9
35-44	25	21.3	29	20.6	17	16.1	54	21.0	71	19.7
45-54	48	35.7	32	33.1	26	27.7	80	34.6	106	32.7
55-64	79	59.5	57	55.3	41	46.0	136	57.6	177	54.4
65-74	85	85.0	72	83.3	62	73.7	157	84.2	219	81.3
75+	50	100.0	43	100.0	59	100.0	93	100.0	152	100.0
Sample Size	333		257		224		590		814	
Mean Age	57.67		59.37		62.31		58.41		59.48	

Note: AM is acute myeloid or monocytic leukemia; CM is chronic myeloid or monocytic leukemia; and OTH includes all non-lymphatic leukemia cases for which one of the above diagnoses could not be made.

The category AM and CM is referred to as M-type leukemias, and the AM, CM and OTH category is referred to as non-lymphatic leukemia, in the text.

Table 19.

Tri-State Leukemia Survey - Age Distributions

Kolmogrov-Smirnov Test values under hypothesis of common underlying distributions

Relative Cumulative Frequencies Compared	D Value	Prob.
Census vs. AL	16.4	.00
Census vs. CL	57.7	.00
Census vs. AM	35.6	.00
Census vs. CM	38.2	.00
Census vs. OTH	43.6	.00
*AM vs. CM	4.5	>.20
Census vs. AM and CM	36.7	.00
Census vs. AM, CM and OTH	38.6	.00
T_5 vs. AM, CM and OTH	4.0	>.10
T_6 vs. AM, CM and OTH	-3.8	>.10

* This was a two sample test. All others are one sample tests since total census data gives accurate frequency information.

The last two line of Table 19. show the close agreement between the two theoretical curves posited in Table 17. and the actual observed curve representing observed non-lymphatic leukemia cases in the Tri-State Survey. It should be noted that all three survey areas had tumor registries, so that virtually all of the leukemia cases diagnosed over the three year period were included in this study.

The control sample used for the Tri-State Survey was based on a stratified selection of households, chosen prior to the start of interviewing. Study areas were stratified into census tracts in cities and into ennumeration districts in rural and suburban areas. This was done on the basis of U.S. census information. All information was initially collected in a double-blind interview, to prevent bias. If the inter-viewer discovered that the person interviewed had leukemia, this was noted in the schedule at the point of identification. There were extensive re-interviews for reliability checks, and independent verification of verbal reports. Each interview involved, on the average, two calls at a household. Some required as many as ten calls. There was a 12% refusal of interview, in the initial telephone contacts, but this was later reduced to 8% after personal contact with the selected subjects was made.

Further detailed information on the Tri-State Survey is available in scientific literature (8). It is internationally recognized as an excellent data base.

Of particular interest to my testimony on diagnostic X-ray exposures, are the verification techniques used when the person interviewed reported such exposure. At the end of each interview the person was asked to sign a statement granting the study personnel permission to review their medical records in physicians offices and hospitals. Only about 1% refused this permission. Cooperation from physicians and hospitals was excellent, 69% responding with the first request, 15% more with the second request. The remaining 13% were contacted by telephone.

Eventually when all records were in on medical X-ray received by the persons included in the sample, it was found that about 80% of the X-ray given by physicians and dentists, and about 67% of that given in hospitals had not been reported by the interviewee. There was also 19.3% of the reports of X-ray by physicians or dentists, and 42.9% of the reports of X-ray in hospitals which could not be verified. Much of the lack of verification was due to a policy, set by the doctor or hospital, of destroying patient X-ray records after five years.

It is obvious that reliance on interview data alone, without verification would have made the study completely invalid. Reliance on verified X-ray only runs the risk of some under-reporting due to the verification itself. A decision was made prior to my involvement in the study, to confine the analysis to verified reports only. I feel that in view of the important findings on radiation, and in view of the national attention being given to this hazard at the present time, a new data processing should be initiated which would allow for assessment of all X-ray reports. The method of analysis which I have used, since it involved an evaluation of each case and control individually, is probably best suited to the type of data with which I had to work.

Table 20 gives the number and percent of the non-lymphatic cases and controls having verified X-ray reports. With one exception, discussed later, there is no evidence that the verification procedure selected out cases at a higher rate than controls.

Table 20.

The Number and Percent of Non-lymphatic Leukemia Cases and Controls in each Age Group Having Verified X-ray

Age Cases	Males No.	Males %	Females No.	Females %	Combined No.	Combined %
15-24	7	30.4	3	25.0	10	28.6
25-34	14	48.3	12	48.0	26	48.1
35-44	26	74.3	16	44.4	42	59.2
45-54	31	53.4	31	64.6	62	58.5
55-64	62	58.5	41	57.7	103	58.2
65-74	82	59.0	45	56.3	127	58.0
75-	39	50.6	41	54.7	80	52.6
Sum	261	55.9	189	54.5	450	55.3

Ages Cntrls	Males No.	Males %	Females No.	Females %	Combined No.	Combined %
15-24	55	51.9	53	63.9	108	57.1
25-34	36	50.0	40	70.2	76	58.9
35-44	21	38.9	79	71.2	100	60.6
45-54	85	64.4	71	70.3	156	67.0
55-64	106	63.1	86	57.7	192	60.6
65-74	56	59.6	82	61.7	138	60.8
75-	22	52.4	32	47.1	54	49.1
Sum	381	57.0	443	63.1	824	60.1

Figures 2,3 and 4, in the main part of the testimony show the cumulative relative frequencies of the non-lymphatic leukemia cases with verified X-ray, against the previously determined expected values by age, determined by the entire non-lymphatic sample. The verification process did not significantly alter the age pattern. The over-representation of male cases in the 35-44 age group with verified X-ray accounts for the slight deviation in the male curve. The combined male-female sample is well within the expected boundaries, which were based on observation of both verified and unverified X-ray exposure cases.

Table 21. gives the estimates of incidence rate for non-lymphatic leukemia in the general surveyed population, using the controls to estimate the proportion of the base population expected to have verified X-ray reports. Except for the male CM leukemia, verification seems to be selecting populations with slightly less non-lymphatic leukemia than is true for the whole population. Under-estimation is greatest for the females.

Table 21.

NUMBER OF LEUKEMIA CASES PER 100,000 IN THE POPULATION AS ESTIMATED FROM THE TRI-STATE LEUKEMIA SURVEY FOR PERSONS WITH AND WITHOUT VERIFIED X-RAY (ADULTS ONLY)

Leukemia Type	**Male Rate per 100,000/yr.**		**Female Rate per 100,000/yr.**	
	With Verified X-Ray	**Without Verified X-Ray**	**With verified X-Ray**	**Without verified X-Ray**
AM	0.99	1.15	0.61	0.74
CM	0.82	0.62	0.55	0.64
OTHER	0.62	0.78	0.31	0.73
All Non-lymphatic	2.43	2.55	1.48	2.12

The time distribution of the exposure to diagnostic X-ray is of special importance in clarifying the relationship between exposure and clinical manifestation of disease. In the coding of the data three time periods were designated, all measurements dating back in time from the date of interview for controls, and the date of diagnosis of leukemia for cases:

1. one to five years prior;
2. six to ten years prior;
3. eleven or more years prior.

There was no verified X-ray more than twenty years prior to either diagnosis or interview. The period of exposure and the average Roentgen skin dose X-ray per year during that time period gives some indication of the exposure pattern of the general public in 1960. Appendix II will address some of the changes in pattern of exposure for the U.S. population since 1960. In the averages given in Table 22., only periods in which X-ray is actually received are included. Since it can be assumed that a time period without verified X-ray is a true radiation free period if there is verified X-ray reported prior to it, one can estimate that at least 28.6% of the control had such an X-ray free period. About 14% of the males, and 18% of the females reported X-ray exposure in all three time periods. This group also had the highest R per year exposure rate.

Table 22.
Time Distribution for Medical X-ray exposure for Tri-State Leukemia Survey Controls, Together with Average R Skin Dose Exposure

Time Intervals	Average R Skin Dose per Year in Interval					
	Male		Female		Combined	
	No.	R/yr.	No.	R/yr.	No.	R/yr.
1 only	141	1.266	154	1.386	295	1.330
1 and 2 only	78	1.471	80	1.308	158	1.388
1, 2 and 3	55	1.661	80	1.904	135	1.805
1 and 3 only	39	0.792	34	1.165	73	0.966
2 only	27	0.480	45	0.680	72	0.604
2 and 3 only	11	0.479	18	0.771	29	0.660
3 only	30	0.870	32	0.972	62	0.922
Average for all periods in which there was verified X-ray	381	1.21	443	1.32	824	1.27

In view of the findings reported in Table 11., of this testimony, I examined the time of exposure for males in the 31 to 44 year age group. In this group, 53% of the cases reported exposure during the second time period, 6-10 yrs. prior to diagnosis. The corresponding male controls reported only 32% in the second time period. While this is not conclusive, it is in line with the expected lag time between exposure and clinical manifestation of disease. I also noted that there was a higher percentage of former military personnel among the cases between 35 and 44 years, than among the corresponding age group of male controls. In view of the present search for military personnel involved in nuclear weapon testing, this could be an important find. These rather nebulous clues have not been followed up partly because not all of the information contained in the Tri-State Data is coded and on tape, and partly because of administrative limitations on access to the data.

The Tri-State Data has the potential of answering most of the questions presently being debated relative to exposures to low level radiation. I refer primarily to the threshhold hypothesis, the shape of the dose-response curve at low levels, and the relationship between dose and dose rate. In order to do this a complete re-coding and processing of the data is mandatory. While the present retrievable information on site of X-ray is in four categories: chest, abdomen, extremities, and other (dental), the information available gives exact site. With respect to chronic diseases discussed in the testimony, the date of diagnosis for each is given in the file folder, but is not available on tape. The same is true for each verified X-ray. The sequence of these events is of the utmost importance in attempting any further analysis of this data.

I would also suggest that more than one researcher be designated to analyze this data. The broadest and most creative approaches are needed, and this means cooperation and sharing of insights, rather than professional competition.

Appendix II - Trends in diagnostic X-ray Exposure:

For completeness, I am adding a short appendix giving information on the basic trends in the use of medical X-ray since the completion of the Tri-State Leukemia Survey. Since this information is generally available through the Department of Health, Education and Welfare, I have strictly limited my presentation. The body of my testimony dealt with my own experience and analysis, and this could not be gotten from any other source at this time.

Table 23 gives the skin dose (mR in air at skin entrance), and bone marrow dose (mrad) for common diagnostic X-ray procedures. Except for spinal and some abdominal X-ray procedures, these exposures are within present guidelines for exposure of the public to ionizing radiation. Such guidelines, while not applying to the medical use of X-ray, have certainly affected people's concept of "safe".

In declaring these doses "unsafe", I am also claiming that routine emmissions from nuclear industries are unsafe for people. The problem of worker exposure is, of course, even greater.

While the exposure per film has been reduced for most X-ray procedures, the rate of X-ray examinations per 100 persons has increased. Table 24 shows the increases per type of examination,and Table 25 the increase for each age and sex grouping. The number of plates used for each examination adds to the exposure problem, and Table 26 gives an estimate of bone marrow dose per examination, rather than per plate.

Table 23.

Estimated Skin and Bone Marrow Dose From

Diagnostic X-ray

Body Area	Skin Dose in mR Average per film 1960	1970	Bone Marrow Dose per film in mrad (1970)
Head/Neck	279	300	12.8 - 24.0
Thoracic Spine	1265	980	10.8 - 65.7
Chest	45	44	0.75 - 6.82
Abdomen	790	960	8.5 - 200.6
Pelvis	829	610	7.93 -296.46 (to fetus)
			5.73 - 53.68
Limbs	117	100	0.17 - 1.2
Dental	1138	910	0.65 - 2.44

Data in the above table was compiled from:

"Population Exposures to X-ray U.S. 1964"

"Population Exposure to X-ray U.S. 1970" DHEW Publ. (FDA) 73-8047

"Organ Doses in Diagnostic Radiology" DHEW Publ. (FDA) 76-8030

"The Mean Active Bone Marrow Dose to the Adult Population of the U.S. from Diagnostic Radiology" DHEW Publ. (FDA) 77-8013

TABLE 24.

Table E-1. Estimated examination rates by type of radiographic examination and sex, United States, 1964 and 1970

Type of examination	Number per 100 persons							
	Male				Female			
	1964		1970		1964		1970	
	Rate	S.E.	Rate	S.E.	Rate	S.E.	Rate	S.E.
Skull	1.7	0.6	2.5	0.4	1.5	0.6	1.7	0.3
Cervical Spine	1.1	0.3	1.7	0.4	1.6	0.6	1.5	0.3
Chest								
Radiographic	18.1	2.0	25.3	1.3	16.7	1.8	23.4	1.2
Photofluorographic	8.4	1.3	4.5	0.6	8.9	1.3	5.8	0.6
Thoracic Spine	0.8	0.5	0.7	0.2	0.6	0.4	0.8	0.2
Shoulder	0.8	0.5	1.0	0.3	0.8	4.6	1.0	0.3
Upper Gastrointestinal Series	3.1	1.9	3.4	0.5	2.9	0.8	3.4	0.5
Barium Enema	1.4	0.6	1.6	0.4	1.8	0.7	1.9	0.4
Cholecystography or Cholangiogram	1.2	0.6	1.6	0.4	1.8	0.7	2.4	0.4
Intravenous or Retrograde Pyelogram	2.0	0.7	2.0	0.4	1.5	0.6	1.9	0.4
Abdomen, KUB, Flat Plate	2.2	0.7	1.7	0.4	1.0	0.5	1.7	0.3
Lumbar Spine	2.2	0.7	3.1	0.5	2.1	0.7	2.4	0.4
Pelvis	1.2	0.6	0.8	0.3	1.1	0.6	1.3	0.3
Hip	0.5	0.4	0.4	0.2	0.7	0.5	1.0	0.3
Upper Extremities	4.9	1.1	5.7	0.6	3.4	0.9	4.1	0.5
Lower Extremities	7.0	1.3	6.4	0.7	4.0	1.0	5.7	0.6
Other Abdominal Exams	0.8	0.3	0.6	0.4	1.0	0.5	1.2	0.5
All Other	2.3	0.8	2.7	0.8	1.5	0.6	2.2	0.7

DHEW PUBL. (FDA) 76-8034

TABLE 25.

Table E-2. Estimated number and rate of radiographic examinations by age and sex, United States, 1964 and 1970

Age & sex	Number in thousands				Number per 100 persons			
	1964		1970		1964		1970	
	Exams	S.E.	Exams	S.E.	Exams	S.E.	Exams	S.E.
Both sexes	104,987	4,619	129,070	2,904	56.2	2.5	64.6	1.5
under 15	14,865	1,665	16,462	938	25.2	2.8	28.0	1.6
15-29	27,771	2,333	28,637	1,231	59.9	5.0	60.8	2.6
30-44	23,194	2,087	25,849	1,163	66.8	6.0	76.9	3.5
45-64	32,314	2,520	39,443	1,459	85.4	6.7	95.5	3.5
65 & over	11,842	1,516	18,679	1,009	69.2	8.9	98.4	5.3
Male								
under 15	9,095	1,346	9,275	733	30.3	4.5	31.0	2.4
15-29	12,020	1,533	15,131	908	66.5	8.6	67.5	4.1
30-44	11,697	1,497	12,825	846	70.5	9.0	79.4	5.2
45-64	16,776	1,745	17,627	987	92.0	9.6	89.7	5.0
65 & over	4,553	997	8,450	718	60.2	13.2	104.5	8.9
Female								
under 15	5,770	1,096	7,186	661	19.9	3.8	24.9	2.3
15-29	10,751	1,430	13,506	864	53.9	7.2	54.7	3.5
30-44	11,497	1,483	13,025	860	63.5	8.2	74.6	4.9
45-64	15,538	1,678	21,816	1,091	79.4	8.6	100.7	5.0
65 & over	7,290	1,225	10,229	767	76.4	12.8	93.8	7.0

DHEW Publ. (FDA) 76-8034

TABLE 26.

Table 3. Mean active bone marrow dose to the adult population (1970)

Examination	Mean active bone marrow dose per examination (mrad)	Annual per capita examination rate	Annual per capita dose (mrad ± S.E.)	
HEAD AND NECK				
Skull	78	0.020		1.6 ± 0.1
Cervical Spine	52	0.022		1.2 ± 0.2
Other	—	—		0.6 ± 0.2
THORAX				
Chest-photofluoro.	44	0.073		3.2 ± 0.3
Chest-radiographic	10	0.300		3.2 ± 0.1
Thoracic Spine	247	0.010		2.5 ± 0.4
Ribs	143	0.009		1.3 ± 0.2
Other	—	—		1.9 ± 0.4
UPPER ABDOMEN				
Upper GI Series (total)	535			24.3 ± 4.7
Radiographic (subtotal)	294	0.046	13.5 ± 4.3	
Fluoroscopic (subtotal)	241	0.045	10.8 ± 1.9	
Scan	167			
Spot Films	74			
Lumbar Spine	347	0.023		8.1 ± 0.8
Gall Bladder (total	168			3.7 ± 0.4
Radiographic (subtotal)	129	0.027	3.5 ± 0.3	
Fluoroscopic (subtotal)	39	0.006	0.2 ± 0.3	
Scan	29			
Spot Film	10			
Small Bowel Series	422	0.002		1.0 ± 0.3
Other				2.1 ± 1.0
LOWER ABDOMEN				
Barium Enema (total)	875			21.2 ± 1.8
Radiographic (subtotal	497	0.024	11.9 ± 1.0	
Fluoroscopic (subtotal)	378	0.024	9.3 ± 1.5	
Scan	268			
Spot Films	110			
IVP	420	0.024		10.1 ± 0.[illegible]
Lumbosacral Spine	430	0.013		5.7 ± 0.7
Abdomen KUB	147	0.020		2.9 ± 0.4
Other	—	—		0.4 ± 0.2
PELVIS				
Pelvimetry	595	0.002		1.4 ± 0.5
Pelvis	93	0.012		1.1 ± 0.2
Hip	72	0.009		0.7 ± 0.1
Other	—	—		1.2 ± 0.7
EXTREMITIES				
Femur	21	0.002		0.04 ± 0.02
DENTAL	9.4	0.312		2.9 ± 0.2
				TOTAL 103 ± 5

DHEW PUBL (FDA)
77-8013

BEST COPY AVAILABLE

Efforts to reduce the number of plates used per examination can be expected to significantly reduce the exposure rate for the individual. The common practice in ordinary photography of taking an extra picture in case the first picture does not prove satisfactory, should never become an X-ray policy! Trained, licensed X-ray technicians can reduce the number of repeat X-rays needed.

The impact of insurance, medicare and medicaid on X-ray policy needs also to be investigated. Research grants involving X-ray techniques used on a-symptomatic persons, or on diseased persons whose treatment cannot be improved by further X-ray information, need scrutiny.

A whole generation of Americans have been told wrongly that low level radiation is not a health hazards, and all of the subsequent wrong decisions which have been made on the basis of this wrong information now need to be reversed. The place to begin this reversal is with medical X-ray, but this is by no means the eradication of the problem!

Dr. Rosalie Bertell

References:

1. DHEW Publication (FDA) 77-8013. "The Mean Active Bone Marrow Dose to the Adult Population of the United States from Diagnostic Radiology." Table 6, pp 19-20 (1964 estimates).
2. DHEW Publication. "Population Exposure to X-ray United States 1964". Appendix B.
3. Gibson,R.; Graham,S.; Lilienfeld, A.; et.al. "Irradiation in the Epidemiology of Leukemia among Adults." Journal Nat. Cancer Inst. 48:2; 301-311.
4. Viadana,E; Bross,I.D.J. "Use of Medical History to Predict the Future Occurrence of Leukemias in Adults." Preventive Medicine 3, 165-170 (1974).
5. Bertell,R. "X-ray Exposure and Premature Aging." Journal of Surgical Oncology 9: 379-391 (1977)
6. DHEW Publication No. (HRA) 77-1457. "Statistics Needed for Determining the Effects of the Environment on Health."

Journal of Surgical Oncology 9:379–391 (1977)

X-Ray Exposure and Premature Aging

ROSALIE BERTELL, Ph.D.

An hypothesis of an aging effect of exposure to ionizing radiation in humans is proposed and given precise mathematical expression. The assumption is made that the biological changes which occur when humans are exposed to ionizing radiation from medical x ray are comparable to those occurring through the natural aging process, since both factors are known to increase the relative risk of nonlymphatic leukemia. This assumption focuses on this one aspect of aging only. The hypothesis that aging and exposure to ionizing radiation are comparable for increasing the relative risk of nonlymphatic leukemia is tested against the data from the Tri-State Leukemia Survey. It is shown to explain the data in a statistically acceptable way, giving an estimate of 1 rad skin dose exposure to the trunk as comparable to 1 year natural aging. This research raises further questions concerning the effects of exposure to ionizing radiation, and presents a new methodology by which these questions may be researched.

Key words: x ray, aging, leukemia, radiation

INTRODUCTION

There has long been speculation in scientific circles that the biological effect on humans of exposure to ionizing radiation is comparable to the effect of normal aging. Dr. Elkaleg (1966), well-known student of both radiation effects and gerontology, has gone so far as to state:

> "Gerontologists have shown keen interest in the effect of chronic exposure to very small doses of radiation. Many believe that this phenomenon may prove to be the key to our understanding of the normal aging process." (p. 895).

Research into mortality and morbidity rates of diseases for persons chronically exposed to low doses of ionizing radiation has shown significantly high rates for cancer (especially leukemia), diabetes, cardiovascular-renal disease, stroke, and hypertension (Gibson et al., 1972; Lea, 1947; German, 1974; Matanoski et al., 1975a, 1975b; Seltser

From the Roswell Park Memorial Institute, Buffalo, New York

Text of presentation at the national meeting of American Public Health Association, 2:00 p.m., Tuesday, November 18, 1975. Sponsored by the Radiological Health Section.

Address reprint requests to Rosalie Bertell, Ph.D., Roswell Park Memorial Institute, 666 Elm Street, Buffalo, NY 14263.

©1977 Alan R. Liss, Inc., 150 Fifth Avenue, New York, NY 10011

and Sartwell, 1965; Burnet, 1974). The conclusion reached by Seltser and Sartwell (1965) in their study of mortality of American radiologists relative to other medical specialists was as follows:

> "These findings warrant the inference that occupational exposure to ionizing radiation on the part of physicians has in the past produced a nonspecific life-shortening effect." (p. 22).

Research presented in this paper moves this speculation into a precise and testable hypothesis. It provides a model for testing the theory that exposure to ionizing radiation has a primary effect of accelerating the natural aging process, and that the observed increase in incidence rates for various chronic diseases among persons exposed to radiation is "normal" for their altered biological age. This model is applied specifically to the relation between exposure to ionizing radiation and the occurrence of nonlymphatic leukemia, as reported in the Tri-State Leukemia Survey.

Bridging the gap between a speculative and nebulous theory and a precise hypothesis which could be tested against a reliable body of data is an important first step in understanding the complex biological interaction between man and his environment. It moves a theory from the hypothetical to the real world.

The data from the Tri-State Leukemia Survey probably represent the best available retrospective data on diagnostic x-ray exposure for leukemia cases and randomly selected controls (Graham et al., 1963). Information on the number of x-ray plates used and site of x ray is converted to the average rads skin dose x-radiation received under standard American diagnostic procedures current in 1959–1962, the time during which the survey was administered. Using this data base, an estimate of the aging effect relevant for today's medical procedures was obtained.

In this analysis, only verified reports of diagnostic x-ray received 1 year or more prior to diagnosis for cases and to interview for controls is considered. The time interval over which the exposure is reported is 20 years, with the bulk of the reporting within the first 10 years prior to diagnosis.

Reconciliation of the findings reported in this paper with the large body of literature relative to the question is not attempted in this paper. A fresh look at previous data reports in the literature reveals no fundamental contradictions, and some clarifications of reported effects of radiation which could not, at the time of writing, be explained. There is some difficulty with the expression "life-shortening effect," which is frequently taken as an averaging over the whole population of the years lost by the premature death of some members of the population. This is not the same concept used here. Life-shortening effect or aging as used here refer to the stress on the individual which undermines his biocommunication facility, reducing his ability to cope with life and maintain healthy homeostasis. Such breakdown is associated with debilitating illness prior to death and actual premature termination of life.

FORMULATING THE HYPOTHESIS

Most theories of biological aging posit a breakdown in biofeedback, so that gradually the organism becomes unable to cope with the stresses caused by daily living. Whether the information needed to trigger an appropriate reaction to restore well-being is totally absent or is blurred (an "error" message, or misinformation), the result is the same. It is well known that the biochemical carriers of information in the human organism are subject to alterations with time and with exposure to ionizing radiation (Lea, 1947. German, 1974). There may well be more than one identifiable bioinformation system, and the gradual breakdown of one such system may be associated with a syndrome of clinical manifestations.

Key to recognizing the similarity in the results of aging and of exposures to low level x ray is the undramatic, hardly perceived but cumulative damage which results from each. We do not seem to be dealing with extensive cell damage and destroyed tissue, but rather with injured cells able to continue functioning and even reproducing themselves within the body. Because of nonrepair or misrepair of slight damage, these cells introduce error into some biological information system. When the error level reaches a certain point, it becomes clinically observable in terms of some inability of the organism to control the internal environment and restore homeostasis.

In terms of leukemia, this is manifested as an inability to maintain a normal cell population in the blood.

The question posed is the following: Can an increase in age proportional to amount of ionizing radiation received be shown to account fully for the significant increase in relative risk of nonlymphatic leukemia in a real sample of cases and controls with known exposures? As in any scientific inquiry, if the real data reject the hypothesis, the question is settled in the negative. When the real data support the hypothesis, further research is required and the hypothesis must be taken into consideration with respect to past scientific-medical experience and with respect to plans for future protection of public health.

Since it is valid to hypothesize that both natural aging and exposure to low levels of ionizing radiation bring about a comparable gradual breakdown in the biofeedback mechanism which may be clinically manifested as leukemia, it should be possible to devise a simple way to test the validity of this hypothesis. Mathematically expressed, we can posit the existence of a number k_e, and calculate for each person an exposure age, e, as follows:

$$e = c + k_e r$$

where c is the person's chronological age and r is the number of rads skin dose of ionizing radiation to which he or she has been exposed. We then posit as a testable hypothesis that persons of the same exposure age have the same probability of contracting leukemia. In effect, we are saying that exposure age e measures both aging and radiation exposure in interchangeable quantities. For example, if $k_e = 1$, a person 45 years old with 15 rads skin dose exposure to ionizing radiation would have the same probability of contracting leukemia as a person 58 years old with 2 rads skin dose exposure. Both would have exposure age 60, and it would matter little whether the "age" was acquired in the natural course of events or through the exposure.

The Tri-State data provided the reliable information with which to test the hypothesis and evaluate k_e. Since the nonlymphatic leukemia types have shown a strong relation to radiation for males over 45 years of age, this subgroup of cases and controls was used as the first test of the hypothesis against factual human data (Gibson et al., 1972). An age effect hypothesis would be expected to be either more clearly acceptable in this group or more easily rejected. If the hypothesis proves acceptable, the technique could then be used to more carefully explore other subgroups. The research design required fully accounting for the increased relative risk of nonlymphatic leukemia in this subgroup by an age shift for both cases and controls, directly proportional to the skin dose of x ray to the trunk, which each had received. See Appendix A for further technical discussion of the measurement of radiation exposure relative to verified information available in the Tri-State survey.

THE TRI-STATE DATA

The Tri-State Leukemia Survey was administered in selected areas of New York State, Maryland, and Minnesota, between 1959 and 1962. All reported cases of leukemia and a random sample of controls were interviewed. The population base for the study was about 13 million, and the random sample controls were chosen at a rate of approximately 1 per 3,000.

The adult sample of the survey, those 15 years and older, includes 1,400 leukemia cases and 1,370 random controls. Detailed information on disease history, mobility, exposures to suspected hazards, and personal history was gathered (Gibson et al., 1972; Graham et al., 1963). Verification techniques included contacting all medical personnel, hospitals, and laboratories mentioned. Detailed information on the site and number of diagnostic x-ray plates taken was obtainable for about half of the sample, and only such verified reports were used in this study. Verification techniques could not be shown to have introduced any bias with regard to age distribution or diagnostic x-ray exposure for cases or controls.

Table I gives the age distribution by leukemia type in the Tri-State Survey data. The acute lymphatic leukemia cases were eliminated from the present adult study because the preponderant occurrence of this type of leukemia is in children. The chronic lymphatic leukemia cases were eliminated both because the age distribution of these cases significantly differed from that of the myeloid and monocytic type of leukemia cases, and because this type of leukemia has never been shown to be radiation-related. The etiology of the lymphatic leukemias appears to be different from that of the myeloid leukemias.

Because of further limitations on the data imposed by the requirement that subjects be male, over 45 years of age, with verified trunk x ray, it was important to attain the largest possible sample size for cases. Since the Kolmogorov-Smirnov test (Siegel, 1956) showed the age distributions to be homogeneous, it was decided that the sample of nonlymphatic leukemia cases could be pooled. This includes all leukemias not diagnosed as either acute or chronic lymphatic leukemia.

Table II gives the age distribution of the base population from which the Tri-State information was collected.

Table III gives the D values, the maximum difference in percent between the two cumulative relative frequency curves being compared. The probability of a D value this large or larger occurring under the homogeneity hypothesis is given.

TESTING THE AGING HYPOTHESIS

If the hypothesis of equivalent effect for natural aging and exposure to diagnostic x ray is acceptable, then when cases and controls of the "correct" exposure age are compared, i.e., when k_e is found, the incidence rates of nonlymphatic leukemia for those reporting more x-ray exposure should be the same as the incidence rate for those not so exposed. This would mean, in terms of our previous example, that the 45-year-old man having 15 rads of exposure to ionizing radiation would not have a greater relative risk of nonlymphatic leukemia than the 58-year-old man having 2 rads exposure. In some way

TABLE I. Age Distributions by Leukemia Type – Tri-State Survey

	AM		CM		OTH		AM and CM		AM, CM, and OTH	
Age	No.	Relative cumulative frequency	No.	Relative cumulative frequency	No.	Relative cumulative frequency	No.	Relative cumulative frequency	No.	Relative cumulative frequency
15–24	19	5.7	9	3.5	7	3.1	28	4.7	35	4.3
25–34	27	13.8	15	9.3	12	8.5	42	11.9	54	10.9
35–44	25	21.3	29	20.6	17	16.1	54	21.0	71	19.7
45–54	48	35.7	32	33.1	26	27.7	80	34.6	106	32.7
55–64	79	59.5	57	55.3	41	46.0	136	57.6	177	54.4
65–74	85	85.0	72	83.3	62	73.7	157	84.2	219	81.3
75+	50	100.0	43	100.0	59	100.0	93	100.0	152	100.0
Sample size	333		257		224		590		814	
Mean age	57.67		59.37		62.31		58.41		59.48	

Notes: AM is acute myeloid or monocytic leukemia, CM is chronic myeloid or monocytic leukemia, and OTH includes all nonlymphatic leukemia cases for which one of the above diagnoses could not be made.

The categories AM and CM are referred to as M-type leukemias, and the AM, CM, and OTH categories are referred to as nonlymphatic leukemias in the text.

TABLE II. Age Distribution Based on 1960 Census Data for Areas Involved in Tri-State Leukemia Survey

Age	Number of persons	Relative cumulative frequency
15 - 24	2,183,654	16.8
25 - 34	2,301,104	34.5
35 - 44	2,502,232	53.7
45 - 54	2,287,864	71.3
55 - 64	1,869,281	85.7
65 - 74	1,273,975	95.5
75+	583,860	100.0
Σ	13,001,970	

TABLE III. Tri-State Leukemia Survey – Age Distributions. Kolmogrov-Smirnov Test Values Under Hypothesis of Common Underlying Distributions

Cumulative relative frequencies compared	D Value	Probability
Census vs AM	35.6	.00
Census vs CM	38.2	.00
Census vs OTH	43.6	.00
AM vs CM*	4.5	> .20
Census vs AM and CM	36.7	.00
Census vs AM, CM, and OTH	38.6	.00

*This was a two-sample test. All other are one-sample tests since total census data give accurate frequency information.

their experience may be considered comparable, whether acquired by exposure to time or exposure to ionizing radiation. To test this hypothesis, age adjustment for radiation exposure must be made for each case and each control, using for each the same k value. It must also be shown that, with this adjustment, persons having greater exposure to ionizing radiation no longer have greater relative risk of leukemia than others in their exposure age cohort. What has previously been reported as a radiation effect could then be equally well explained as an aging effect. The usual measure of the ratio of incidence rate of disease among those with high exposure to radiation relative to those with low exposure, namely the relative risk statistic, is used (Bertell, 1975a, 1975b; Cornfield, 1950/1951). A relative risk of one indicated that the incidence rates of disease in the population exposed to more ionizing radiation and in the population not so exposed are the same.

It is possible to predict the behavior of the relative risk statistic as the value of k changes, where k is the estimate of years of aging per rad exposure. If k is taken to be zero, *i.e.*, no age adjustment is made for exposure, we would expect to have a risk of disease in the exposed group relative to the unexposed group of greater than one. Under the aging hypothesis, this is because the exposed persons are biologically in an older age bracket where disease incidence rate is higher. This increased risk would also be true for $k = 0$ if radiation exposure were directly related to leukemia.

As k increases through a set of values k_i, we obtain for each k_i a new set of ages for each case and each control: $e_i = c + k_i r$. This will slightly alter the cohorts matched for comparable age. Under the aging hypothesis, each increase in k brings each individual case and control closer to "true" biological age, which is assumed to be the determining factor in incidence rate for nonlymphatic leukemia. If, however, radiation has a unique random effect not comparable to aging, such age adjustment would not eliminate this effect. We would expect the relative risk for higher exposure to ionizing radiation vs lower exposure either to remain elevated or to change in a random way. What we are then looking for is quite demanding of the real data, namely, one value of k which, when used to adjust the ages of each of the cases and controls in the sample, will eliminate (reduce to one) the increased relative risk of nonlymphatic leukemia with increased exposure to ionizing radiation.

Under the age hypothesis, if k is "too large," the age shift assumed is too great, and we expect the risk of disease in the exposed group relative to the unexposed group to be less than one. This is because the exposed group is biologically younger than others in the given classification, therefore having a smaller incidence rate of disease. Again, if radiation damage is independent of age, this continual decrease in relative risk would not be expected.

The test consists in observing the behavior of the relative risk statistic as k increases through small positive values. Monotonic decrease of relative risk through one supports the aging hypothesis. Persistently high relative risk or random changes would reject the aging hypothesis. Thus theory is examined in the light of real data.

Table IV gives the results of the analysis of the risk of nonlymphatic leukemia for males exposed to 5 or more rads skin dose from trunk x ray, relative to those exposed to less than 5 rad skin dose. Each line in Table IV summarizes an analysis of the total sample, 269 male controls and 214 male nonlymphatic leukemia cases. The first column indicates the value of k, the assumed aging per rad of exposure, which was used in calculating the exposure age of each case and control. Each summary relative risk is a composite of the relative risks within cohorts matched for exposure age. See Appendix A for the discussion of rad skin dose assigned to diagnostic procedures. The rad skin dose was used so that the results of the analysis could be interpreted in terms of current medical diagnostic procedures. The rad unit is also basic to dialogue with health physicists who are evaluating the effects of industrial exposures to ionizing radiation.

Table IV clearly conforms to the pattern predicted under the aging hypothesis. In fact, it is so remarkable that the reader may mistakenly think it is inevitable. The acceptable range of k values is found by noting the probabilities associated with a χ^2 test of the exposure-age-adjusted summary table. This is the probability of the occurrence of the relative risk because of random variation. The values of k between the two horizontal lines cannot be rejected on the 5% level. The k value marked with an asterisk is the estimate of k_0 for this body of data, namely, $k_0 = 0.60$.

In order to test the stability of the estimate of aging effect, i.e., of acceptable k values at even higher levels of radiation exposure, the entire analysis was repeated using as the exposure group those who had received 10 or more rads skin dose, and then repeated again using those who had received 15 or more rads skin dose.

As can be seen in Fig. 1, there is a stable band of values for k, between $k = 0.60$ and $k = 1.45$, which is common to all three analyses. The point estimate, $k_0 = 1$, i.e.,

TABLE IV. Relative Risks of Nonlymphatic Leukemia for Males Over 45 Years of Exposure Age With Trunk X-Ray Exposures of 5 or More Rads

No. years aging per 1 rad exposure	Age-adjusted relative risks	Probability
0.00	1.57	.0017
0.05	1.56	.0022
0.10	1.51	.0036
0.15	1.44	.0101
0.20	1.36	.0295
0.25	1.31	.0522
0.30	1.23	.1220
0.35	1.21	.1558
0.40	1.16	.2706
0.45	1.06	.6489
0.50	1.03	.7952
0.55	1.03	.7718
0.60*	1.00	.9797
0.65	0.99	.8869
0.70	0.94	.5978
0.75	0.93	.5253
0.80	0.92	.4436
0.85	0.90	.3839
0.90	0.94	.5678
0.95	0.92	.4392
1.00	0.93	.5078
1.05	0.91	.4003
1.10	0.89	.3138
1.15	0.90	.3348
1.20	0.88	.2145
1.25	0.87	.2009
1.30	0.86	.1787
1.35	0.85	.1325
1.40	0.84	.1138
1.45	0.82	.0513
1.50	0.79	.0323
1.75	0.76	.0071
2.00	0.74	.0020
2.25	0.71	.0004

*For this body of data k_e = 0.60.

1 rad skin dose exposure to the trunk is equivalent to 1 year natural aging, is a statistically acceptable explanation for the occurrence of nonlymphatic leukemia among those exposed to ionizing radiation. Key to understanding the significance of this finding is the observation that no greater aging per rad needs to be assumed to account for increased leukemia among those exposed to more than 15 rads than for those exposed to more than 10 rads. This is true, although for k = 0, i.e., for no exposure age adjustment, the relative risk of nonlymphatic leukemia for persons having more than 10 rads exposure is 2.00, with probability 0.00, and the relative risk for persons with more than 15 rads exposure is 2.35, with probability 0.00. Both risks decrease with increases in k, and both become 1 at k = 0.95.

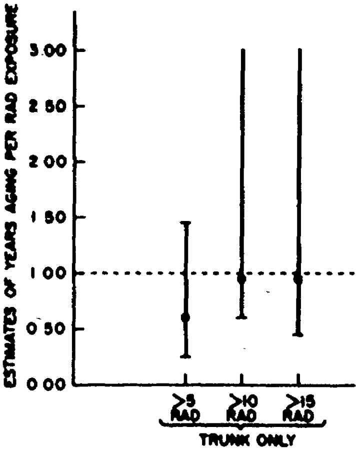


Fig. 1. Statistically acceptable estimates for the rad skin dose (mR in air at skin entrance) equivalent to one year natural aging, for the Tri-State Survey data. Each line represents a 90% confidence interval for k_e using the indicated cut-off.

The slight discrepancy between the first analysis and the two using higher rad exposure levels may be explained by noting that the cases and controls reporting higher levels of exposure were also those reporting abdominal x ray. The value of k_e would be expected to rise under the supposition that irradiation of major components of the hemopoietic system was the relevant exposure involved in the etiology of leukemia. The k value is remarkably stable and the age shift accounts for the previously reported increased relative risk of leukemia with exposure to medical x ray in a statistically acceptable way.

What seems clear, then, is that it is possible to account totally for the radiation-related increase in relative risk of nonlymphatic leukemia in this data by a simple and well-defined age shift which depends on the level of exposure only. For trunk exposure in males aged 45 and older, this age shift is most probably between 0.60 years and 1.45 years per rad skin dose. The easily remembered formula "1 rad is equivalent to 1 year natural aging" is consistent with my findings.

DISCUSSION

This analysis would have been impossible without precise information on each case and control. Prospective studies and human surveillance systems designed to evaluate environmental hazards need similar careful design if they are to yield meaningful information. This has many implications for gathering of routine health statistics. Such fine analysis cannot be carried out using vital statistics as presently collected and published. An adequate gathering of factual data is required to test further the implications of these results.

A second implication of this study has to do with methodology. If we wish to answer the epidemiological questions of the 1970's, we must update our statistical methodology and discover creative new uses of standard techniques. These new approaches to statistical methodology are needed so that the increased precision of information is not lost because of inadequate mathematical techniques, and scientific hypotheses are not neglected because they are not formulated with analytical precision.

The questions of excessive use of diagnostic x ray and the combination of medical exposure with excessive environmental pollution must be faced as important public health problems requiring immediate national attention.

Implications of this study for medical use of diagnostic x ray, especially when the purpose of such patient exposure is to further basic research or to prevent malpractice suits, are serious. It seems advisable to begin steps immediately to curtail unnecessary x rays or x rays not directly beneficial to the person receiving them. Patient records should show a cumulative account of all diagnostic x ray received, including dental. Informed patient, or guardian, consent should be required before each exposure.

Analyses of other radiation-related diseases, such as coronary, atherosclerosis, cataracts, and various solid tumors, in a way comparable to this study of nonlymphatic leukemia, are needed. These studies would perhaps clarify some of the mechanisms of aging, as well as reveal the more generalized effects of ionizing radiation. It is imperative that the effects of low level radiation on humans be further researched before we implement elaborate diagnostic x ray techniques and/or make an irrevocable commitment to pollute the environment further with hazardous radioactive material.

Appendix B has been added to give the mathematical reader a deeper insight into the underlying theory which prompted this research and the future directions which measurements of low level radiation effects may be expected to take.

APPENDIX A

Coding of the verified diagnostic x-ray data in the Tri-State Survey includes the exact number of plates used in medical examinations of four body sites: teeth, chest, abdomen, and extremities. The latter category included head and neck examinations.

For the purpose of this paper, the two categories, chest and abdomen were selected. In the years since the survey was collected there has been a change in the radiation exposure in terms of rads skin dose per plate for these examinations; hence a conversion from number of plates to rads skin dose was indicated. This conversion provides a more meaningful tool of communication, not subject to the variations noted in the measurement by plate.

Conversion of number of x-ray plates used to rads skin dose received was based on estimates for medical practice in the United States for 1960 made by the Bureau of Radiological Health, Department of Health, Education and Welfare (Gitlin and Lawrence, 1966). Abdominal x-ray conversion was 790 mrad skin dose per plate. No overall estimate of rads skin dose per chest x-ray plate is given, so a weighted average assuming that 90% of such exposures were standard chest radiographic examinations of the lungs, and 10% were cervical or thoracic spine or other upper trunk examinations, was used. These percentages were reported for the general public, and were verified for a random sample of the Tri-State Survery. An estimate of 167 mrad skin dose x-radiation was used for each verified chest plate reported.

Further research involving estimates of bone marrow dose per diagnostic procedure would be expected to yield further information on the etiology of leukemia.

There is also evidence that irradiation of the liver and spleen, or other specific organs, may be of special biological interest with respect to aging. A recoding of the Tri-State Survey information would be needed to answer these questions.

APPENDIX B

The original insight into the equivalence of 1 rad exposure to ionizing radiation and 1 year of natural aging came through the fortuitous applications of a newly developed mathematical technique to both aging and exposure to diagnostic trunk x ray. This new technique will be presented in detail in another paper "On estimating leukemia risk per x-ray plate," which is in preparation. It was designed to quantify an increase in relative risk of disease for exposure to an environmental hazard which admits of measurable degrees, such as numbers of x-ray plate exposures, packs of cigarettes smoked per day, years of natural aging, etc.

Application of the mathematical theory to trunk x-ray exposure and to natural aging showed an increase in relative risk of nonlymphatic leukemia of 5 to 6% with each plate and/or year. The striking similarity was not immediately accepted as indicative of equivalence, but was used rather to formulate a precise hypothesis which could be rigorously tested in the manner described in the body of this paper.

For the reader interested in the technique involved in quantifying the relative risk of nonlymphatic leukemia per year of aging, a brief explanation is given here.

Table II gives the age distribution according to the 1960 census for the appropriate areas from which the Tri-State survey data were drawn. From this distribution two theoretical distributions, T_5 and T_6, were derived; T_5 and T_6 represent cumulative relative frequency functions assuming a relative risk of $(1.05)^t$ and $(1.06)^t$ of leukemia for t years beyond 15 (Table V). The theoretical expected frequencies are obtained as follows:

From the relative frequencies in the census data, we determine that p(20) = 0.168

TABLE V. Theoretical Cumulative Relative Frequency Curves for Relative Risks $(1.05)^t$ and $(1.06)^t$ for t Years Beyond 15*

Age	T_5	T_6
15-24	3.6	2.4
25-34	9.7	7.1
35-44	20.5	16.0
45-54	36.7	30.7
55-64	58.3	52.2
65-74	82.2	78.4
75+	100.0	100.0

*This table is derived from Table II, the age distribution of the population from which the Tri-State information was drawn. See text for explanation of the methodology involved in the derivation.

is the probability of being in the 15–24-year age category; $p(30) = 0.177$ is the probability of being in the 25–34-year age category, and so on.

Under the hypothesis that the relative risk of leukemia for each year of natural aging is 1.05, the probabilities for the cases are obtained:

$$q(20) = \frac{(1.05)^{5}\, p(20)}{S}$$

is the probability of a case being in the 15–24-year category, and

$$q(30) = \frac{(1.05)^{15}\, p(30)}{S}$$

$$q(40) = \frac{(1.05)^{25}\, p(40)}{S}\text{, and so on,}$$

where S is the sum of all the numerators. The cumulants can then be formed.

This definition conforms to the usual meaning of relative risk or odds ratio, since the odds for getting leukemia in the 25–34-year age category relative to the 15–24-year age category would be

$$\text{R.R.}^{*} = \frac{q(30)\, p(20)}{p(30)\, q(20)} = (1.05)^{10}.$$

Figure 2 shows the observed cumulative relative frequency function for the cases against the band predicted when there is a 5 to 6% increase in relative risk with each year of natural aging.

The deviation of the cumulative relative frequency function of the combined acute myeloid, chronic myeloid, and nonlymphatic leukemias could not be distinguished statistically from the predicated curves T_5 and T_6, based on a relative risk of (1.05) and (1.06) per year of natural aging, with the Kolmogorov-Smirnov test (Siegel, 1956). The maximum deviation between the cumulative relative frequency curve of the cases and the theoretical curve T_5 was +4.0; its maximum deviation from T_6 was −3.8. Both values are acceptable random deviations, in a 90% confidence interval. Separate analyses for males and females showed consistent and similar results.

The comparison of the subsample of those cases with verified x-ray reports and the census data revealed no age bias caused by the verification procedure.

ACKNOWLEDGMENTS

The highly sophisticated computer software which made this analysis possible was patiently developed by Dr. Leslie Blumenson, Chandu Rathod, and Tom Rzepka. The author is indebted to them, and to Dr. Augustine Ball, Susan Kovacs, and Mary Ann Kuczmarski for much clerical and stenographical assistance. Dr. Irwin Bross, Department Chairman, provided the atmosphere, encouragement, and critical stimulation which made this creatively different approach to the radiation data possible.

This investigation was supported by Grant Number CA-11531, awarded by the National Cancer Institute, Department of Health, Education and Welfare.

---

*R.R. is the ratio of disease incidence in one subgroup of a population to the disease incidence in another subgroup. As used here, the subgroups are persons 25–34 years old and persons 15–24 years old.

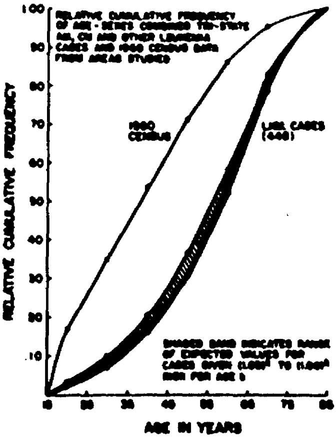


Fig 2. Mathematical model for predicting the age distribution of the leukemia patients in the Tri-State survey Leukemia types are as noted in Table I.

REFERENCES

Bertell, R (1975a) Extensions of the relative risk concept Experientia 31:1–10.

Bertell, R (1975b) An alternate method for calculating an odds ratio. J. Med. 6(1):15–26.

Burnet, M. (1974) "Intrinsic Mutagenesis A Genetic Approach to Aging." New York: Wiley.

Cornfield, J. (1950/1951). A method of estimating comparative rates from clinical data. Applications to cancer of the lung, breast and cervix. J. Natl. Cancer Inst. 11:1269.

Eikeles, A. (1966). Atherosclerosis and radioactivity. J. Am. Geriat. Soc. 14:895–901.

German, J. (editor) (1974) "Chromosomes and Cancer." New York: Wiley.

Gibson, R , Graham, S , Lilienfeld, A., Schuman, L., Dowd, J. E., Levin, M. L. (1972). Irradiation in the epidemiology of leukemia among adults. J. Natl. Cancer Inst. 48(2):301–311.

Gitlin, J. N. and Lawrence, P. S. (1966). Population exposure to X-rays, U.S. 1964, U.S. Dept. of Health, Education and Welfare, Publication No. 1519. Washington, D.C.: U.S. Government Printing Office.

Graham, S , Levin, M. L., Lilienfeld, A , Schuman, L., Dowd, J. E., Levin, M. L. (1963). Methodological problems and designs of Tri-State leukemia survey. Ann. N. Y. Acad. Sci. 107:557–569.

Lea, D. A. (1947). "Actions of Radiation on Living Cells." New York. Macmillan.

Matanoski, G. M , Seltser, R., Sartwell, P. E., Diamond, E. L., and Elliott, E. A. (1975a). The current mortality rates of radiologists and other physician specialists: Specific causes of death. Am. J. Epidemiol. 101(3):199–210.

Matanoski, G. M., Seltser, R., Sartwell, P. E., Diamond, E. L., and Elliott, E. A. (1975b). The current mortality rates of radiologists and other physician specialists: Deaths from all causes and from cancer Am. J. Epidemiol. 101(3):188–198.

Seltser, R., and Sartwell, P. E. (1965). The influence of occupational exposure to radiation on the mortality of American radiologists and other medical specialists. Am. J. Epidemiol. 81:2–22.

Siegel, S (1956). "Nonparametric Statistics." New York: McGraw Hill, pp. 47–52, 127–136

Mr. Rogers. Thank you. What we will do, I am going to have the staff go over this very carefully, and we may want to get back to you with additional questions. This is excellent work and certainly needs to be done, because I don't think I have ever seen this done before.

Dr. Bertell. I am sure you haven't.

Mr. Rogers. That is excellent. I commend you.

Our next witness now will be Rose Kushner, who is director of the Breast Cancer Advisory Center.

STATEMENT OF ROSE KUSHNER

Ms. Kushner. Thank you, Congressman Rogers, for inviting me. This in an abbreviated form of my prepared written statement.

I am a breast cancer patient, and I am also the executive director of the Breast Cancer Advisory Center. This is a nonprofit medical-service organization that I began in 1975. Since then, mammography—X-rays of the breast—has been a top priority question, and I have had to learn a lot about it. Most attention has been paid by everyone to the 27 breast cancer detection demonstration projects, or BCDDP's, which are still in existence. Contrary to what Dr. Laws thought, these have not been discontinued. They are still operating, sponsored jointly by the National Cancer Institute and American Cancer Society.

Although these projects receive most of the publicity, there are only 27 mammographs and 280,000 women in them. In my opinion, this program is just one blatant example of mismanagement and misuse of X-ray and not a major issue by itself. According to the Bureau of Radiological Health (BRH), there are about 4,000 to 5,000 pieces of equipment out there in the United States being used to X-ray women's breasts. These are either mammographs specifically designed for breasts or they are general purpose machines that have been properly modified for this use.

But in addition to these thousands of appropriate mammographs, general purpose X-ray machines are still being used to study breasts, machines that were neither designed for nor modified for this purpose. No one really knows how many there are in this general purpose category, but the Bureau estimates that about 30 percent of all mammography being done in this country today is being performed with such equipment.

Since there are about 50 million women in the vulnerable age groups in this country and so many X-ray machines used to detect possible breast cancer, the relative insignificance of the 27 detection centers and the 280,000 women enrolled in them can be appreciated. These few detection centers are now rigorously patrolled and monitored by six full-time radiation physicists: twice as many as the number covering all radiation—ionizing and nonionizing—for the entire State of Maryland, my home State. The personnel employed to take the X-rays in the BCDDP's are certified, qualified and licensed. This leaves millions of us to the mercy of unmonitored equipment and, often, unqualified technologists. There are more of us than there are in the BCDDP's, but nobody seems to be paying any attention to the rest of us.

Before going any further, I would like to stress there is a vital distinction between the kind of X-ray screening done in those

Projects and what is known as diagnostic mammography. This distinction cannot be emphasized enough because the publicity and confusion generated by the mammography controversy has frightened women to the point where those with obvious reasons to be X-rayed are refusing mammography. There has never been any controversy about being mammographed for diagnosis of a symptom. If a woman has a symptom of what might be breast cancer, she should be mammographed. The only controversy has evolved around the kind of screening to which Dr. McClenahan referred. If a malignancy is so small that it cannot be felt, and that is screening, not diagnosis mammography. Screening is a subject of much controversy.

There is also no difference of opinion, as far as I know, about mammography for women like me, who have already lost one breast to cancer, or for women who have a strong family history of the disease. In such instances, the risk that something is wrong now by far outweighs any fear that the radiation may cause or accelerate the growth of a malignancy in future years.

Breast cancer is the chief killer of women between the ages of 44 and 55 in the United States, because it is usually not diagnosed until it has already spread, or metastasized, to other parts of the body. In the 1930's, scientists began to hope that X-rays could detect cancers in breasts before they could be felt, and by the 1960's, mammography had been refined enough to be a reliable aid to physical examination.

In 1963, the Health Insurance Plan of Greater New York, HIP, began a comparative study to see if mammography actually lengthened women's lives. After 7 years, the HIP statisticians found there was a significant difference, in women over age 50, in mortality rates between the two groups. These 1971 results were impressive enough to convince the American Cancer Society and the National Cancer Institute to cosponsor the screening centers, and the first ones were established in 1973.

The main goal was simply to see if 270,000 women would volunteer to be X-rayed routinely for breast cancer. For this reason, I have been told, the women were self-selected rather than randomly assigned, as they were in the HIP program.

There was some worry about possible radiation risks, but Dr. Frank J. Rauscher, Jr., then the Director of the NCI, calmed the fears, even though the National Academy of Sciences had already issued the so-called BEIR report: The Biological Effects of Ionizing Radiation in 1972. This document details the increased incidence of breast cancer in three populations of irradiated women.

In addition, the Bureau of Radiological Health had done a few studies of mass-screening programs by mammography, and the Bureau opposed such programs for a variety of reason. However, the founders of the BCDDP's did not, for reasons I cannot understand, ask for advice from our radiation watchdogs. And neither the National Academy of Sciences nor the Bureau of Radiological Health volunteered any information. Government agencies, I discovered, do not invade each others turfs.

To get back to the BCDDP's, any fear that the needed 280,000 women would not volunteer evaporated in the fall of 1974 when Mrs. Betty Ford and Mrs. Happy Rockefeller were treated for breast cancer. In no time at all, the needed women enrolled for the free annual examinations, and we were all assured that the X-rays used for screening were of such low dosages that they would do no harm.

Behind the scenes, however, there were many opponents to these programs, even though we women did not know anything about the opposition at the time. Then, in the spring of 1975, Dr. John C. Bailar III, the editor of the Journal of the National Cancer Institute, made the opposition public for the first time. Only then did we find out what was going on. After that, there was a considerable public fuss with coverage by all the media.

The National Cancer Institute restricted the use of mammography for screening, in the projects only, to women of age 50 and to certain populations of high-risk women; the equipment, film, personnel and usage, came under tight control and inspection by six radiation physicists.

Before going on, I would like to point out that the "rad" is the abbreviation of radiation-absorbed-dose. As far as the breast is concerned, this is computed to the quantity of radiation at the midpoint of the breast. Obviously, since women's breasts vary considerably—size, age, whether or not they have ever been pregnant, have breast-fed children, et cetera—there is really no way to know with any degree of certainty how many rads a particular woman's breast is absorbing at its midpoint. The reason I am stressing this right now is that we women are constantly being bombarded with miscellaneous maxima of rads we should permit, when no one really knows the exact figure we should be getting. The quantity of X-ray that may be able to give an excellent image of one woman's breast may be dangerously insufficient for another. To expose a woman's breast to such a safe, low dose of X-ray that an existing cancer will not be seen on the film is, to say the least, counterproductive. So there is really no magic number of rads for every woman. A 36 double-D sized (brassiere) breast needs a different quantity of radiation than does a triple-A. Now that the furor about the BCDDP's is subsiding, I hope somebody will begin to give some thought and attention to the rest of us women out in the country: The tens of millions not now being given tender loving care by the National Cancer Institute.

Probably the most dangerous fallout from all this radiation-blast is that thousands of women who should be X-rayed are refusing mammography. I am sure the National Cancer Institute has the data concerning the number of women who have dropped out.

As the director of the Breast Cancer Advisory Center, I know that thousands of women have refused mammography when they should be getting it. Women are afraid, because they don't know what is safe. Even for diagnostic X-rays, we have the right to feel confident that we are being exposed to as little ionizing radiation necessary, consistent with a high-quality reliable and accurate image. At this time, we have no such assurance even when mammography is definitely indicated. In the State of Maryland where I live, for example, there is a board of cosmetologists—and I have their rules and regulations here—that dictates how and by whom my hair can be washed and cut, my nails manicured and my lipstick demonstrated in a department store. All of these people need to be licensed in Maryland.

There is also an environmental protection department that sees to it that my butcher does not short-weigh my salami and steak and that my supermarket's scales charge me accurately for the pounds of fruit and vegetables I buy. But the State of Maryland has no such authority over the X-ray machines, that might be zapping me with ionizing irradiation, or over the personnel operating them.

To be sure you don't label me a female chauvinist, I must remind the subcommittee this lack of regulatory authority applies to X-ray of males as well.

There are only five States—New York, New Jersey, California, Kentucky, and Arizona—as well as Puerto Rico, that require X-ray technologists, the critical people who decide what dials to turn, what buttons to push, to be licensed.

In the United States, there appears to be a motley array of State programs that go from stringent—for example, California requires physicians who use X-ray and radiologists to be recertified on a regular basis—to almost nothing. The grand total of radiation control personnel in all the 50 States and the entities—Puerto Rico, Guam, Samoa, Virgin Islands, and Washington, D.C.—is only 350. These people are responsible for all uses of radiation—ionizing and nonionizing—and so I really do not think the individual States can be expected to do much more without Federal support and money.

What is the Federal Government doing? Our chief watchdog over radiation is the Bureau of Radiological Health, an agency that was created within the FDA in 1968. Another agency that is mandated to look after radiation of Federal facilities is the Environmental Protection Agency, and I understand the Department of Defense looks after radiology in military hospitals.

If I sound unclear as to who is minding what store, it is because I am unclear as to who is minding what store. Regarding mammography—and I am only talking about diagnostic mammography right now—I will concern myself only with the Bureau of Radiological Health, because I know most about it.

The Bureau has total control over equipment in the factory and over installation and assembly in any office, clinic or hospital where it is to be used. This means that Bureau of Radiological Health inspectors can—and do—order mammographs that do not meet compliance standards to be sent back to be corrected and adjusted until they do meet the compliance standards.

According to the testimony of Mr. John Villforth, the Bureau's Director, before a Senate hearing last year, 30 to 50 percent of all X-ray equipment has to be returned either before shipment from the factory or after installation in the ultimate destination because it does not meet compliance standards.

This sounds great: New equipment must meet certain standards. However, the Bureau has no authority to inspect equipment that was already in use prior to 1974, just 4 years ago.

I have already told the subcommittee that there are about 4,000 to 5,000 machines out there being used to X-ray our breasts and that the Bureau estimates that about 30 percent of these are general purpose machines, never having been modified to focus only on the breasts. Of course, these are in the majority, since X-ray has been around for decades. To protect women—and men—adequately, all equipment—its compliance in manufacture and assembly and its continuing inspection—must be under the regulation of the Bureau of Radiological Health.

Of course, such continuing regulation has no value if the BRH has no authority to penalize abusers. Like Maryland's Board of Cosmetology, which can fine or close the shop of a noncomplying haircutter, the Bureau needs some teeth to be able to enforce its regulations. It also needs money to pay those teeth, because today, our watchdog has toothless gums.

The film used by radiologists to take X-rays of the breast was, in the past, high dose and required a great deal of radiation to get a good quality, reliable image. Now more than 90 percent of all mammograms are being done with low-dose film. We women are gratified to know about this change, but film is only one of the factors contributing to accurate, reliable, good quality images that expose women to as little ionizing radiation as is necessary.

Perhaps the best way to explain the fractional role the film plays in the process is to compare mammography with ordinary picture taking. A photographer can have a Nikon, Leica or Brownie Instamatic. The film can be very fast, requiring little light—which is like roentgens of ionizing radiation—or very slow—requiring a lot of light. The critical factor in the picture taking equation is the skill of the photographer. I know that, except for a lucky accident, I and my Nikon—using the best of film on the sunniest of days—could not take as good a photograph as a skilled photographer using an inexpensive Brownie Instamatic.

The radiation technologist is the analog of the photographer. Once upon a time—and Dr. McClenahan is still doing it, but he is rare—it was common for radiologists themselves to first examine their patients so they could know their density and estimate their size and decide how many KVP's and MAS's were needed to get a good image with as little radiation as possible. But according to the FDA testimony given to the Senate last year, one-third of the estimated 150,000 technologists actively employed now in the United States are not credentialed.

This means that about 50,000 radiation technologists, the people who determine our radiation exposures—men's as well as women's—are not required by any law to do anything to prove they know how to operate the X-ray equipment.

As I said earlier, my State of Maryland has strict regulations governing cosmetologists. An operator is required to take at least 1,500 hours of classes and must pass a written as well as a performance examination. Only then can a haircutter receive a license. Manicurists and shampooers and cosmetic demonstrators must also be licensed. However, in Maryland, anyone can walk off the street and operate a mammograph legally. Of course, most hospitals and many physicians do require certification, but this is voluntary. They are not required by the laws of the State of Maryland.

I have gone into such detail to show the importance of modern, well-maintained equipment operated by qualified personnel because there has been so much brouhaha from opponents of regulation about low-dose film. There is no question that low-dose film is better than high-dose film, but we women still have no way of knowing if we are being zapped by antique equipment under the control of untrained, unqualified technicians. What we need is a seal of approval, telling us that the equipment is in top condition, and a diploma on the wall, giving us confidence that the technologist has had some instruction in its use. We do not have that now.

The Bureau of Radiological Health does have a mammography quality assurance program—BENT—which I am sure you will hear about in the next few days. This is a free program but it is also voluntary. Sometimes I think having BENT is better than having nothing at all; sometimes I am afraid the progam misleads women into thinking that the Government is regulating radiologists. Under these circumstances, BENT may be doing more harm than good.

[Testimony resumes on p. 173.]

[Mrs. Kushners' prepared statement follows:]

ROSE KUSHNER

9607 KINGSTON ROAD
KENSINGTON, MARYLAND 20795
(301) 949-2530

11 July, 1978

Congressman Rogers and other distinguished members of this Subcommittee:

Thank you for inviting me today to present my views -- as an informed patient -- on the use of medical radiology.

My name is Rose Kushner. As I have already indicated, I was diagnosed and treated for breast cancer in 1974. In addition I am the executive director of the Breast Cancer Advisory Center -- a non-profit medical service organization founded in 1975 to help women who have problems regarding breast disease. I began the BCAC after publication of my book, now titled Why Me?, made me aware of the great need for some kind of an information clearinghouse where women could turn for help before the disease is found. Diagnosis via mammography -- X-rays of the breasts -- obviously was and still is a top-priority question, and I had to learn a good deal about this technique in order to help the almost 10,000 women (and their families) who have turned to the Breast Cancer Advisory Center for help.

However, before addressing myself specifically to this kind of X-ray, I would like to comment, wherever I feel qualified, on the questions sent to me by the Subcommittee prior to these hearings.

A. I believe that enough evidence has been presented by both researchers and clinicians to show that there has been considerable radiation-induced damage and disease from low-level ionizing radiation. From what I have learned as a result of the "mammography controversy" -- which I will detail later -- I believe medical practices will only be changed by some kind of governmental regulation, regulation that gives the regulators the power to penalize abusers;

B. I accept the Food and Drug Administration's estimates regarding unnecessary X-rays, although I would guess that these are conservatively low. It seems impossible to legislate medical judgment regarding when an X-ray is needed, but certainly legislation can see to it that we patients are exposed to as little ionizing radiation possible, consistent with a good image. "Incentives" guaranteeing that this will be done, in my opinion, should be penalties if it is not;

C. Most of the questions in this section deal with issues I do not feel competent to address. Again, I stress that regulation by law -- with penalties for repeated violation -- will solve many problems caused by poor equipment and unqualified personnel. As for education aimed at related medical professionals and the public, such education cannot be force-fed. I have seen much of the literature prepared and distributed by government agencies, and what I have seen is excellent. However, unless the various professions themselves begin to police their memberships and require continuing education and periodic recertification, physicians, technologists, nurses, etc. will probably do as little as necessary to learn new findings and data. For the public, I believe the general mass media -- especially television and popular newspapers like the National Enquirer -- can do more than all the government handouts put together. There is little question that the audiences of major television programs and weeklies are huge, but these have not been considered "educational" routes. What little has been presented by television has been so obviously "educational" in the form of documentaries that mass audiences are not attracted. The same is true for serious books and lengthy, in-depth articles. In my opinion, a great deal of public education could and should be incorporated into "soap operas," situation comedies and dramas, confession magazines and even into comic-book plots. Of course, this kind of public-education programming cannot be legislated in a free society any more than medical judgment can be legislated. But perhaps it could be encouraged by the miscellaneous public-information officers of the agencies.

At this time, I will leave the Subcommittee's list to concentrate on the area of medical diagnostic radiology I know most about -- mammography. In the course of discussing breast X-rays, many of the points listed will be addressed, and -- perhaps -- my ideas will also apply to other kinds of radiology.

Most attention has been paid by the Congress, the media and the public to the 27 Breast Cancer Detection Demonstration Projects (BCDDPs) sponsored jointly by the National Cancer Institute and the American Cancer Society. Although the BCDDPs have received most of the publicity, these few mammographs and the 270,000 women who are involved in the Projects are -- in my opinion -- simply one example of blatent mismanagement and misuse of X-ray. According to the Bureau of Radiological Health (BRH), there are about 4,000 to 5,000 pieces of equipment being used in the United States to X-ray women's breasts. These are either mammographs specifically designed for breasts or are "general purpose" machines that have been properly modified for this use. (Xerograms are reproduced on paper instead of film but are still considered to be mammography, and both methods rely on ionizing radiation.)

But, in addition to these thousands of appropriate mammographs, "general purpose" X-ray machines are still being used for breasts, machines that were neither designed nor modified. No one knows precisely how many there are in this category, but the

BRH estimates that about 30 per cent of all the mammography being done in the country today is being performed with such equipment.

When one considers that there are about 50 million women in the vulnerable age groups in the United States and so many X-ray machines being used to detect possible breast cancer, the relative insignificance of the 270,000 enrollees of the BCDDPs can be appreciated. These 27 Detection Centers are now being rigorously patrolled and monitored by six full-time radiation physicists, and the personnel employed to take the X-rays are certified, qualified and often licensed. But this leaves millions of us women to the mercy of unmonitored equipment and often unqualified technologists. There are more of us than of those in the BCDDPs, but no one seems to be paying much attention to the millions of women who are not lucky enough to be cared for by the 27 Centers.

However, since the BCDDPs are so well-known, I will go into their history briefly to illustrate how the issue began in the first place. Before going any further, I would like to stress that there is a vital distinction between the kind of "screening" by X-ray done in the BCDDPs and what is known as "diagnostic mammography." This difference cannot be emphasized enough, because the publicity and confusion generated by the "mammography controversy" has frightened women to the point where those with obvious reasons to be X-rayed are refusing valuable mammography. The only "controversy" has revolved around X-raying the breasts of women who have no reason whatsoever to believe they may be growing a malignancy too small to be felt or diagnosed by any other method. If a woman has any symptom of what might be breast cancer, the X-ray is "diagnostic" -- not "screening" -- and there has been no difference of opinion about using ionizing radiation in such cases. The same is true for women like me, who have already lost one breast to cancer and for those who have strong family histories of the disease. In all such instances, the risk that something is wrong, by far, outweighs any fear that the radiation may cause or accelerate the growth of a malignancy in later years.

Breast cancer is the chief killer of women between the ages of 44 and 55 in the United States, because it is usually not diagnosed until it has spread -- metastasized -- to other parts of the body. More than three-fourths of all women undergoing surgery are found to have metastatic spread to the lymph nodes (or glands) of the underarm area, the axilla. In the 1930s, scientists began to explore the notion that X-rays would be able to detect cancers in breasts during their pre-clinical stages, before they could be felt. By the 1960s, diagnostic mammography had been refined enough to be a reliable aid to simple physical examination, even though the equipment was crude and unsophisticated by today's standards.

In 1963, the Health Insurance Plan of Greater New York (HIP) began a comparative study to see if mammography actually lengthened women's lives by detecting breast cancers before they had already invaded other parts of their bodies. Two groups of women were chosen at random: the "study group" received mammography in addition to the regular HIP annual examinations; the "control group" was given every other test and examination except the breast X-rays. After seven years of such screening (Women with symptoms were not included in the "study group."), HIP statisticians found that only 70 of the mammographed women had died of breast cancer, while 108 of the group who had not been X-rayed had died of the disease. The significant difference in mortality rates was attributed to the early detection by the mammograph.

The 1971 results of the HIP study were impressive enough to convince the American Cancer Society and the National Cancer Institute to co-sponsor the BCDDPs, and the first detection centers were established in 1973, with much fanfare. According to statements made in September, 1977 at a Consensus Committee at the National Institutes of Health, the main goal of the Projects was to determine if 270,000 women would volunteer to be routinely X-rayed for breast cancer. For this reason, the women were "self-selected" rather than randomly assigned, and there were other differences between these programs and HIP.

According to statements made by Drs. Philip Strax and Arthur Holleb (initiators of the BCDDPs) before the Consensus Committee, there was some worry about possible radiation risks, but these were calmed by a letter from Dr. Frank J. Rauscher, the former director of the National Cancer Institute.

I would like to mention here that the National Academy of Sciences had issued the so-called BEIR report -- The Biological Effects of Ionizing Radiation -- in 1972. This document detailed the increased incidence of breast cancer in three populations of irradiated women: survivors of the atomic-bombings in Hiroshima and Nagasaki, tuberculosis patients who were frequently fluoroscoped to monitor their disease and women who were X-rayed for mastitis after childbirth. In addition, the Bureau of Radiological Health had done several studies of mass-screening by mammography, and the prevailing opinion opposed such programs for a variety of reasons. However, the founders of the BCDDPs did not -- I have been told -- ask for advice from our radiation watchdogs, and neither the NAS nor the BRH volunteered any information. Government agencies, apparently, do not invade each others' turfs.

To get back to the BCDDPs -- any fears that the needed 270,000 women would not volunteer evaporated in the fall of 1974 when the first and second wives of the United States -- Betty Ford and Happy Rockefeller -- were treated for breast cancer. In no time at all, 260,281 women enrolled for the free annual examinations. The BRH reports were, essentially, "in house memos," requiring no publicity, and the BIER report based its results on massive doses of ionizing radiation. So we women were assured that the X-rays used in screening were of such low dosage that they could do no harm. There was, initially, no "informed consent" statement to be signed, because neither the NCI nor the ACS considered the BCDDPs to be "experimental."

Behind the scenes, in the scientific community, there were many opponents to the BCDDPs, however, even though we women knew nothing about the controversy at that time. In the spring of 1975, Dr. John C. Bailar III, the editor of the Journal of the National Cancer Institute. first made the opposition public in a paper he presented before a medical society, and it was published in January, 1976 -- "Mammography: A Contrary View" -- in the Annals of Internal Medicine. It promptly caused a furor in the general media, a succession of meetings and conferences -- public and professional -- that were covered in great depth by all, and only then did we women find out what was going on. The National Cancer Institute restricted the use of mammography in the BCDDPs only to certain populations of high-risk women, the equipment used came under rigorous inspection and control by radiation physicists, low-dose film became mandatory and no dose was to exceed 0.5 rad per exposure. (It was not unusual, prior to the uproar, for an exposure to give a woman much more radiation.) Personnel, of course, are qualified.

Before going on, I would like to point out that the "rad" is the abbreviation of radiation-absorbed-dose, and -- where the breast is concerned -- this is computed to be the quantity of radiation at the midpoint of the breast. Obviously, since women's breasts vary considerably, depending on size, age, whether or not she has borne and breast-fed children, etc., there is actually no precise way to know with certainty how many rads a particular woman's breast is absorbing at its mid-point. All that a radiologist can know is how many Roentgens a mammograph is emitting, and calculations can then be made to estimate the rads being absorbed. I have been told that the absorbed dose is estimated to be about 25 per cent of the Roentgens. The reason I am stressing this here is that we women are being bombarded with miscellaneous maxima of "rads" we should permit, when no one really knows the figure. The quantity of X-ray that may be able to give an excellent image for one woman may be dangerously insufficient for another. To expose a woman's breasts to such a low dose of X-ray that an existing cancer will not be seen on the film is -- to say the least -- counter-productive; what is appropriate for a 60-year-old women who has breast-fed five children may not be enough for a large-breasted 40-year-old who has never been pregnant. Thus, there is no "magic rad." Yet that is what we are being told.

Now that the furor about the abuses of the BCDDPs is -- I hope -- subsiding, what about the rest of us women out in the country -- the tens of millions not being given such tender-loving-care by the National Cancer Institute?

Probably the most dangerous fall-out from this radiation blast is that thousands of women who should be X-rayed are refusing mammography. The National Cancer Institute has the data regarding the numbers of women who have dropped out of the BCDDPs, even though they meet the criteria of age and high-risk status now required. I, as the recipient of thousands of queries about breast cancer, know that women who have lumps, nipple discharge and other symptoms, as well as women who have already had breasts removed for cancer, are insistent that no X-rays be taken. The publicity that followed the "mammography controversy" has so terrified and confused women that even such essential diagnostic mammography is being rejected. As I stressed earlier, the only arguments have surrounded routine screening of asymptomatic women, and this cannot be emphasized too strongly.

But even for diagnosis, women have the right to feel confident that they are being exposed to as little ionizing radiation necessary, consistent with a high-quality and reliable image. At this time, there is no such assurance. In the state of Maryland, where I live, for example, there is a Board of Cosmetologists that regulates how and by whom my hair is to be washed and cut, my nails manicured and my lipstick applied. There is also an Environmental Protection Department that sees to it that my butcher does not shortweigh my salami or steak and that my super market's scales charge me accurately for the pounds of fruit and vegetables I buy.

The state of Maryland has no such authority over the X-ray machines that might be zapping me with excessive ionizing irradiation. To be sure you do not label me a female chauvinist, I must remind the Subcommittee that this lack of regulatory authority applies to male residents of Maryland as well.

However, there are five states -- New York, New Jersey, California, Kentucky and Arizona -- as well as Puerto Rico, that require that X-ray technologists, the critical people who decide what dials to turn and what buttons to push, are licensed. In addition there appears to be a rather motley array of state programs that go from stringent (California, I have read, requires physicians involved in radiology to be re-certified on a regular basis) to nothing. Since all the radiation-control personnel of the 50 states and the "entities" like Puerto Rico, Guam, Samoa, the Virgin Islands and Washington, D.C. total only about 350 people (who are responsible for all uses of radiation), I cannot feel the individual states can be expected to do much more.

What is the federal government doing?

Well, our chief watchdog over radiation is the Bureau of Radiological Health, an agency that was created within the Food and Drug Administration in 1968. Another agency that is mandated to look after ionizing radiation in federal facilities is the Environmental Protection Agency, and the Department of Defense -- from what I have been told -- looks after radiology in military hospitals. If I sound unclear about who is minding what store, it is simply because I am unclear about these jurisdictional lines and what each federal agency does.

Regarding mammography -- and this is the only diagnostic radiology I will talk about now, although the situation is the same for other types -- I will concern myself only with the Bureau of Radiological Health. This is the agency with which I am most familiar and which appears to dominate.

Under The "Regulations for the Administration Enforcement of The Radiation Control for Health and Safety Act of 1968," the BRH has total control over equipment in the factory and over installation in an office, clinic or hospital where it is to be used. This means that BRH inspectors can (and do) order that mammographs not meeting compliance standards be sent back to the assembly lines to be corrected and adjusted until they meet the standards. According to Mr. John Villforth's testimony before a Senate hearing last year, from 30 to 50 per cent of all X-ray equipment must be returned either from the factory shipping door or from the ultimate destination, because of failure to meet these criteria. The reason the Bureau's inspection mandate continues until X-ray equipment is installed, by the way, is that most are sold as components -- similar to the way high-fidelity sound equipment is sold -- and the assembling process could affect the final outcome, even if the individual segments are totally in compliance with BRH standards.

This sounds great, except that the Bureau has no authority to inspect equipment that was already assembled and in use prior to 1974 -- four short years ago. I have already told the Subcommittee that some 4-5,000 machines out there are being used to X-ray our breasts and that the BRH estimates that about 30 per cent of these are "general purpose" machines that have not been modified to focus only on the breasts. Perhaps someone from the Bureau has precise numbers that would tell you how many of these machines are being used under the 1974 "Grandfather's clause" that is permitting them to X-ray us even though they were never subject to any compliance inspection at all. I have not even been able to get an estimate, but I did interview a veteran radiologist who was using the same equipment he bought when he went into practice 25 years ago. He told me that he expected to retire shortly and did not see any reason why he should invest in any new, fancy gadgets if the law did not require him to. In fairness, I will tell you that he is not using this archaic museum-piece to perform mammography, because -- practicing in a large city -- there is no need for him to do so. He regularly refers women elsewhere for mammography. However, there are areas in the United States where a single X-ray machine is all there is.

Equipment -- its compliance in manufacture and assembly and its continuing inspection -- should be under the regulation of the Bureau of Radiological Health. Of course, continuing inspection in the clinic, office and hospital has no value if the BRH has no authority to penalize abusers. Like Maryland's Board of Cosmetology, which can fine or close the shop of a non-complying haircutter, the BRH needs some teeth to be able to enforce its regulations. Right now, our watchdog has toothless gums.

The film used by radiologists to take X-rays of the breasts was -- in the past -- "high dose" and required a great deal of radiation to get a high-quality, reliable image. Film manufacturers and radiologists have made us all aware of the fact that more than 90 per cent of all mammograms are now being done with "low-dose" film. (This, of course, excludes equipment that reproduces the images on paper -- Xerographs.)

Of course, all women are gratified to know that this change has taken place so quickly. However, the film used is only one of the factors affecting the desired result: an accurate, reliable, good-quality image that exposes women to as little ionizing radiation necessary to obtain it. Perhaps the best way to explain the fractional role the film plays in the process is to compare mammography with ordinary picture-taking. A photographer can have a Nikon, a Leica or a Brownie 'nstamatic; the film can be very fast -- requiring little light (Roentgens of ionizing radiation) -- or very slow, requiring a lot of light. The critical factor in this picture-taking equation is the skill of the photographer. I know that, except for a lucky accident, I and my Nikon -- using the best of film on the sunniest of days -- could not take as good a photograph as a Steichen or an Eisenstadt with an inexpensive Brownie.

The radiation technologist is the analogue of the photographer. Once upon a time, it might have been routine practice for the radiologists themselves to first examine women's breasts, determine their density, estimate their size and decide how many KVP and MAS would be needed to get an excellent image with minimal exposure to ionizing radiation. Once upon a time, this is the way mammography was done, I have been told. Apparently, some radiologists still feel that it is imperative that they themselves make the critical decisions. But this is not the general rule nowadays, and there is no real reason why physicians should take the time to do what a paramedical professional can do -- providing he or she is properly trained and qualified.

According to FDA testimony given to the Senate last year, "At least one-third of the estimated 150,000 technologists actively employed are not credentialed ..." It is not clear from the transcript of this hearing (Radiation Health and Safety, Committee on Commerce, Science and Transportation: U.S. Senate; 16 June, 1977) whether the word "credentialed" is defined as certified by examination or merely licensed by payment of a fee. In any event, it is obvious that about 50,000 radiation technologists -- critical professionals who determine radiation exposures -- are not required by any law to do anything to prove their capability to manage X-ray equipment.

As I said earlier, my state of Maryland has strict regulations governing cosmetologists, and an operator is required to take at least 1,500 hours of classes and must pass a written as well as a performance examination. Only then can a haircutter receive a license. Manicurists, shampooers and cosmetics demonstrators must also be licensed according to Maryland law. But my state is not one of the five that requires anything of radiation technologists, and -- as far as the law is concerned -- anyone can walk off the street and operarate a mammograph. Of course, hospitals and physicians can and do require certification by the American Association of Radiological Technologists, but such requirements are voluntary. Only five states have laws affecting radiological technologists -- the all-important photographer.

I have gone into such detail to show the importance of modern, well-maintained equipment operated by qualified personnel, because there has been so much brouhaha, from opponents of regulation, about the fact that more than 90 per cent of all mammography is now being done with low-dose film. Low-dose is better than high-dose -- there's no question about it. But we women still have no way of knowing if we are being zapped by antique equipment under the control of untrained, unqualified technicians.

What we need is a governmental "Seal of Approval" telling us that the equipment is in top condition and a diploma on the wall to give us confidence that the technologist has had some instruction in its use. We do not have that now. When a woman writes or calls me for information regarding where to go for mammography, I refer her to one of the BCDDPs, because I know that these facilities are carefully operated by the National Cancer Institute. If she does not live near an NCI Detection Center, I suggest she go to the closest teaching hospital where -- I hope -- both the equipment and technologists are at least good. We women simply have no way to know.

In the summer of 1975, the Bureau of Radiological Health began a mammography quality assurance program called BENT -- Breast Exposure: Nationwide Trends. After a Pennsylvania radiation controllerer found that randomly-selected ~~70 private and~~ public facilities were exposing women to an average of 24 Roentgens per exposure, the voluntary BENT program was created by the Bureau to offer free monitoring to radiologists -- with the assistance of state agencies -- on a voluntary basis. Although BENT was slow aborning, it now includes 42 states plus New York city, the District of Columbia, Puerto Rico and Guam. Most radiologists, of course, do not want to over-expose women's breasts (or anyone elses' organs) to excessive ionizing radiation, and there is no question in my mind that BENT will eventually involve the participation of all radiologists using mammography. It is free, easy to do and voluntary. A card is mailed by the Bureau of Radiological Health -- a dosimetry card called a TLD (thermoluminescent dosimeter). This card is to be exposed at the "technique factors normally used for a craniocaudal view of a 'medium-density, medium-size' breast." The card is then returned to the BRH for evaluation, depending on the equipment and film that was used, and radiologists are informed if there are any problems. Theoretically, followup visits to correct the problems are carried out by state radiation controllers, since BENT is a federal program performed with the cooperation of the various state agencies.

Unfortunately, the TLDs are evaluated only once every year, and a reading that could be perfect when the dosimetry card was used might change within a short time for numerous reasons unknown to the radiologist. I am sure there will be witnesses here who are competent to explain these and to give the members of this Subcommittee an idea of how frequently mammography equipment should be inspected. I have been told that such inspections should be done at least every six months, and some radiation physicists have even suggested monthly examinations.

In addition to the long interval between evaluations under the BENT program, participation is entirely voluntary. There are no federal regulations to assure that radiologists will 1) use the TLD, 2) send it in, 3) make the recommended changes. In other words, there are no penalties attached to non-compliance; we women must depend on the cooperation and good will of the radiologist.

When the BENT program began to make headway, I thought that -- at last! -- we would have our "Seal of Approval." However, as it has developed, participation in gives us no guarantees of safety or reliability at all. Often, I think having BENT is better than having nothing at all. At other times, I find myself afraid that participation in the voluntary BENT program misleads women into thinking that these radiologists are adhering to some kind of federal compliance standard. If this is so, BENT may be doing more harm than good.

To summarize, I believe there must be federal inspection of all mammography equipment on a random, spot-check basis, especially including those machines in use prior to 1974. There must be penalties for chronic violations of the 1974 compliance standards. In addition, there must be some kind of minimum training requirements -- be they federal or state -- for radiological technologists, with periodic recertification after they are initially permitted to operate any X-ray equipment. Licensure alone is a money-earning device, not safety insurance, and it is not enough to protect us from unqualified personnel. Although I believe California's requirement that radiologists also be recertified is an excellent idea, I doubt that it is politically possible in most states. Similarly, I believe insurance companies could not police radiology.

Another issue I would like to address is the cost of mammography. In the Washington, D.C. area, the average fee for a 4-view set of breast X-rays is $75.00. I have been told that the cost elsewhere is as much as $150.00. Why? Dr. Philip Strax, one of mammography's staunchest advocates, has given talks to his colleagues to show how mammograms in the Guttman Institute in New York can be done for $10.00. Let us assume that technological genius does soon develop a totally risk-free mammograph and that there will be no fear attached to being screened every year. Most medical insurance companies do not cover screening of any kind, and certainly, the Congress will not pay to screen 50 million women for breast cancer every year. Why can Dr. Strax get excellent mammograms for $10.00 while the cost will continue to be prohibitive for the rest of us? Sometimes I get the odd feeling that we women are having our terror of breast cancer exploited, and I would appreciate hearing from other witness who know more about what mammography should cost.

There is one last danger of mammography I would like to bring up to this Subcommittee, although it is not related to hazards of ionizing radiation. In the 27 BCDDPs, the so-called prevalence rate of abnormal mammograms was as high as ten times the national incidence rate of 7 per cent. During the first years, this astounding difference was attributed to the detection of occult or hidden breast cancers that would have grown, sooner or later. However, the prevalence rate has continued to be much higher than the normal U.S. incidence rate, and I must ask the question: Is the mammograph so exquisitely sensitive that it is picking up atypical cells -- "pre-malignant cells," if you will -- that will never become full-blown cancers at all?

Indeed, the intense analyses conducted of 509 "minimal cancers" found in the BCDDPs, analyses made for the September, 1977 Consensus Committee by a special committee lead by Dr. Oliver H. Beahrs revealed that only 104 were frankly invasive. The remaining 405 tiny "cancers" studied by the pathologists were varying types of atypical lesions that many breast-cancer experts do not even consider to be malignancies at all. As a result, the term "pre-malignant" or "Stage 0" came into wide use to describe these mammography-detected "cancers," and advocates hailed the technique for having picked them up while they were still curable. Well, certainly, atypical cells that are not cancer at all will be cured when they are removed. However, almost all of the 509 women with these minimal lesions were treated with some kind of mastectomy.

I am not attempting to re-open the issue of whether or not there were indeed 66 benign diagnoses or 22 borderlines, etc. All I would like to point out is that it is possible that mammography is finding "cancers" where none actually exist, and we women are losing our breasts for no reason. From what I have been told by pathologists, there is no way to know -- with current technology -- which atypical cells will simply remain atypical, and which are truly pre-malignant and will become frank cancers that might kill us. However, everyone involved must be aware of this potential danger of even totally risk-free mammography: there may be thousands of healthy breasts amputated for nothing.

Thank you,

Mr. **Rogers**. Thank you.

I think I understand now the thrust of your testimony.

Ms. **Kushner**. There is one more comment I'd like to make.

Mr. **Rogers**. If you can give it to me quickly.

Ms. **Kushner**. Two lines. One of the things that came out of those BCDDP studies is that there was a lot of unnecessary surgery: the mammograph may be so sophisticated and sensitive that it is picking up lesions that are atypical and may not be cancerous at all. I would like everyone involved in mammography to know that the treatment resulting from taking breast X-rays may be excessive and unwarranted.

Thank you.

Mr. **Rogers**. Thank you. We appreciate very much your excellent statement.

I might say that this committee, because of the color television radiation emission situation some years ago, went into this. I introduced and we passed what is now the law on radiation health and safety. I believe that now 10 years later we need to review the whole subject matter. That is why we are holding these hearings.

I think some of the points that you have raised, as well as those raised by others, are certainly well made, and the committee hopes to take some action because of these hearings as a backup to the work we did in 1968 because we really have not looked at this question in depth since then. This is most helpful testimony.

Let me just ask this: We have asked you to submit answers to certain questions for the record that we won't go into now; and you have been very patient, all of you, with the committee to permit us to keep you here this long.

Actually, it would appear from the testimony that the use of medical X-rays for diagnostic purposes is not really based on scientific study of their appropriate use; is that correct?

Dr. **Reiskin**. I would say so, with the exception of a few examples that were cited today.

Mr. **Rogers**. If you have any feelings about that, if you would let us know for the record.

I think that is the point that you were making, Dr. Bertell.

Dr. **Bertell**. Yes.

Mr. **Rogers**. That we need to know the results and the medical basis and what have you. I think your point, too, Dr. Reiskin. So this is what we need to have work done on.

Dr. Bertell?

Dr. **Bertell**. I think there is one thing that wasn't covered today that bothers me, and that is, I think this is a part of a bigger problem, and I don't like to see it solved in isolation from the rest of the problem.

I just briefly mentioned the quality of data, but our collection of public health information is so bad that we can't pick up environmental diseases. It is the same story with saccharin and myrex and PCP and PBB. The story is the same, and there is no need to mount a new study for each one. It is a matter of regearing our public health collection of data to pick up chronic diseases morbidity, the environmentally related diseases. They could be and should be picked up now. We have an outmoded system.

Mr. **Rogers**. Yes; I agree. And we are trying also to change that with the legislation on the statistics, the Bureau of Statistics, Center for Health Statistics. We are trying to bring that up to date to begin to respond to some of these problems.

Also in the radiation field, I think we are beginning to bring about a change in attitude and to get action from the governmental agencies and from the agency involved with running radiation installations. Now they are trying to do a better job in keeping the statistics on what is happening. So your point is well made. We will try to do something.

Would you say that generally the views you have expressed today are pretty much held by the practitioners?

Ms. **Kushner**. No.

Mr. **Rogers**. They are not?

Why not?

Ms. **Kushner**. Why not? I don't know.

Dr. **Laws**. I can speak to this. The question of how low levels of radiation affect people is very, very complex. As a result, what we tend to have in the medical community is a denial of problem. Many physicians say:

> Well, there is no proof at the very low levels that there is any problem for my kind of X-ray; you haven't shown me a study, an epidemiological study that shows my kind of X-ray is hazardous therefore, I think my kind is below the threshold and there is no damage below that threshold.

In addition, there are many myths in the medical community about the effects of radiation. I have seen several short articles in dental quarterlies and other journals that say, "Oh, it is no worse than an hour in the sunshine."

The notion that a certain skin dose from ultraviolet radiation and a certain skin dose from X-rays which are equivalent is misleading because ultraviolate is not penetrating; therefore, it does not affect the thyroid and other internal organs.

The misconceptions about radiation effects among professionals provides evidence that there are widespread deficiencies, as Dr. Raskin mentioned; in the education in the medical and dental schools. On the other hand, there are patients like those mentioned by Rose Kushner who think if they have had an X-ray they are going to die of cancer. I get calls from patients late at night who have read some of my consumer materials and they want to tell me exactly what kind of X-rays they have had in the last 2 years, and they ask, "Am I over the threshold yet; am I going to die of cancer?"

Patients don't understand that an increase in risk does not mean they are going to die of cancer, but only that there is an increased probability of getting it. Thus, I think we go from denial of a problem on the part of the medical community to overreaction on the part of patients.

Ms. **Kushner**. I would just like to point out that history shows that scientists have a terrible track record. They told us that estrogens were perfectly safe; they told us we should take X-rays to shrink up our tonsils, thyroid, ringworm, and thymuses. In general, scientists don't have the kind of accurate track record I would bet my money on. Now, they seem to operate in a vacuum where they have forgotten their history.

Mr. ROGERS. Thank you.

Dr. McClenahan, you are a practitioner. Maybe you can comment for us.

Dr. McCLENAHAN. As I hinted, I think, in what I said a moment ago, I am a little bit puzzled as to how legislation is going to reduce this, because really it comes down to commonsense and to judgment, as I think Dr. Carter said, and how this is put across by law or by ordinance, I simply don't know.

It involves education. It comes, I think, as a burden on the medical student in his first year to be taught what X-rays are good for and what they are not good for. A great deal of the teaching of radiology is done by enthusiasts who have written many papers about it, and they tend to discount its weaknesses or its failure.

I think the second major considerations is the matter of cost; the myth that it doesn't cost anything. A patient will call me and say, there is really nothing wrong with me, but doctor so and so wants you to do this or that or the other thing because I am fully covered. Until there can be some brake on that, I think the abuse is going to continue.

Mr. ROGERS. Should medicare and medicaid require the concurrence of the radiologists before any X-ray is given?

Dr. McCLENAHAN. I think that would help, although that sets up some barrier and some disagreement between the radiologists and many doctors who are accustomed simply to dictating what he should do.

Mr. ROGERS. I understand. But I thought, from your testimony now, that is pretty much the way you operate.

Dr. McCLENAHAN. That is, sir, but this is done at risk. This is done at the risk of losing referrals.

Mr. ROGERS. Have you lost any——

Dr. McCLENAHAN. Yes; I have.

Mr. ROGERS. What would you estimate your problem has been?

Dr. McCLENAHAN. It is hard to say because when you reach the age of 63, your practice dwindles a little bit.

Mr. ROGERS. That's young, Doctor.

Dr. McCLENAHAN. Mine is down in the last 3 years by 20 percent, of which I estimate a substantial amount is due to injured feelings by referrers that I haven't always done as I was told.

Mr. ROGERS. In other words, some of the doctors no longer would refer work to you simply because if you didn't think it really was needed, you would not do it?

Dr. McCLENAHAN. That is true.

Mr. ROGERS. What would you estimate the amount of lost income to be that this reduction amounts to?

Dr. McCLENAHAN. I am now giving away a very crucial secret. It has cost me enough to reduce my income tax considerably.

Mr. ROGERS. Well, I won't pursue that; but you say about a third?

Dr. McCLENAHAN. No; I would say—my income tax or my practice? My practice is down roughly 20 percent.

Mr. ROGERS. About 20 percent?

Dr. McCLENAHAN. Yes.

Mr. ROGERS. So I presume all your income is almost down to that extent, too?

Dr. McClenahan. Yes.

Mr. Rogers. Because you didn't necessarily go up on the other X-rays——

Dr. McClenahan. No; I didn't.

Mr. Rogers. I am sure you didn't.

Let me ask this: Dr. Phillips, why don't the schools do a better job teaching, or what should we do in the education of physicians and dentists regarding proper use of X-ray? Should there be a reexamination of this? Should the schools address themselves to this problem? What would be your feeling?

Dr. Phillips. Yes; I think the curriculum in medical schools, at any rate, does not address the problem of radiation hazards sufficiently. We are very proud of how we can find things, and we are prone to emphasize what we can do, but not emphasizing very much the dangers. In the last few years I must be honest and say we have improved this.

Mr. Rogers. It is changing some?

Dr. Phillips. Yes; but I think we have a long ways to go.

Mr. Rogers. I wonder, what are the best organizations to get some action on this? Would it be well to go to the AAMC, for instance? What about the dental schools?

Dr. Reiskin. I think there are some important differences between the problem that exists in medicine and the problem that exists in dentistry.

In medicine, I hope that the bulk of the radiographic examinations that are done are performed by radiologists who have, in fact, completed fairly extensive training after they finish medical school.

Mr. Rogers. May I say, it is my understanding from testimony we have had today that many X-rays are given by technicians who operate in the doctor's office, the radiologist's office, but he may never have known it was given until he is presented with the accomplished fact.

Dr. Reiskin. I think that is undoubtedly true.

Mr. Rogers. Let's find out if that is true first. Would that generally be true, do you think, Doctor?

Dr. McClenahan. Yes; that's true.

Mr. Rogers. Is it true then?

Dr. Reiskin. I think I would still feel more secure as a patient being in the office of somebody who is a trained radiologist than I would if I walked into the office of my neighborhood GP who had no training in radiology but still operated his own X-ray machine or hired a high school girl to operate it for him and did not have the educational background to understand what was being done or how it should be done.

I think in dentistry that is essentially the problem we have because the level of training is so low. Not only is the average dentist unprepared to set a standard, but I think he is also unprepared to supervise the technician who takes the films for him which, in most cases, is somebody who has no training.

Mr. Rogers. First step, you need to get to the dental schools and medical schools of the Nation to begin to change this pattern. Would that be an agreement?

Dr. Laws. And the RT schools.

Mr. Rogers. Radiation technologists.

Dr. **Reiskin**. There is a political problem involved in doing that, though.

Mr. **Rogers**. In what way?

Dr. **Reiskin**. It may be less of a problem in medicine and dentistry. Radiology is not a specialty, and the dean of a dental school or somebody in the ADA had to deal with all of the boarded specialties which have economic and political clout, and don't want to see their turf invaded by somebody with other interests.

Mr. **Rogers**. Are you saying it will have to be a Federal law to require certain standards for——

Dr. **Reiskin**. It is my best guess that until the biological evidence becomes so devastating, no change will be made unless it is legislated.

Mr. **Rogers**. Is there any comment on that; disagreement?

Dr. **Bertell**. I would like to bring up something a little different. That is, from the point of view of a researcher, if you are trying to speak to doctors or dentists, it is very different from trying to speak to health physicists or radiologists or mathematicians. There is a tremendous difference in the jargon used and the kind of presentation. I would say that since January I have really made an effort to go into medical schools, go into hospitals, talk with radiologists and talk to the medical school personnel, and I have found they are very responsive to direct evidence.

They don't want a whole lot of mathematical models. They don't want to deal with that. They don't want to deal with research papers that are in the research journals, but they will deal with a person who is willing to come and willing to try to explain in plain English and show them what happens in the data. They will deal with that and they will respond to it.

Ms. **Kushner**. As a patient, I would like to point out that no one pays much attention to us. We go into a radiologist's office, and we are not told anything except that "it's good for us."

I interviewed a local radiologist who had paid for equipment he bought as soon as he got his residency. He said he wasn't about to invest any more money in it because there is no law against it. I suspect that this is typical of a great many people.

Mr. **Rogers**. Now let me ask this: Is there any requirement that there be a record kept, medical records of a person, of exposures to radiation?

Ms. **Kushner**. No.

Mr. **Rogers**. Should there be?

Ms. **Kushner**. Yes.

Dr. **Laws**. There is a difficulty with that, because it is the dose in rods to radio-sensitive organs rather than the skin exposure in roentgens which provides a measure of biological harm. The skin exposure is not necessarily completely correlated with the organ doses. Organ doses also depend on the quality of the X-ray beam, which depends in turn on such factors as machine type, tube kilovoltage, and the filtration. I am not convinced that actual exposure records would be of value except for research purposes.

Mr. **Rogers**. Dr. McClenahan?

Dr. **McClenahan**. Measuring the dose per examination is technically a very difficult thing to do with any accuracy, but I think the proposal would have some value in at least recording radiographic exams so that if a patient took his record to such and such a hospital or such and such an office and someone looked at it and saw that this procedure had been done 2 days before or 3 days before or had been done six times in the last year, there might be a brake.

Mr. ROGERS. Is there any requirement in a person's record that this be recorded?

Dr. BERTELL. No.

Dr. LAWS. No; not at all. I have encouraged patients to keep their own records, primarily as Dr. McClenahan has mentioned, so that a patient can say "I had this examination 6 weeks ago at such and such a facility."

Mr. ROGERS. Is it a sufficient problem to warrant having it recorded?

Ms. KUSHNER. Yes.

Dr. LAWS. Yes.

Dr. BERTELL. Yes.

Mr. ROGERS. Does anyone disagree with that? Would you let us know what you might suggest for the record; not now, but for the record along those lines?

Is it the feeling of the panel that we should have licensure for anyone who operates an X-ray machine or not?

Ms. KUSHNER. Licensure with recertification requirements—not as a revenue paying device.

Mr. ROGERS. Doctor?

Dr. MCCLENAHAN. I am not sure about that, Mr. Rogers. Rose Kushner has mentioned recertification in California, and yet in California—I think this figure is correct—chiropractors do 6,000 examinations of the back each month. Now, I don't know how much recertification is going to diminish this amount of exposure. I think it is very easily gotten around. Carelessness in technique, carelessness of a technician is very hard to pick up.

Dr. LAWS. I can add to that. I know the Bureau of Radiological Health has done some studies that show that certified technologists do better than uncertified ones, but not much better. Part of the problem is that technologists will tell you that they learned to use gonad shielding and to collimate the beam to the size of the film, but they work under tremendous pressure when their supervisor doesn't seem to care about these things, they don't take time to do them.

I know the Bureau of Radiological Health has also been trying to look at the conditions under which radiologists and technologists work. There is a tremendous problem of communication in large departments between patient and technologist, technologist and radiologist, and radiologist and prescribing physician. It is the most hierarchal arrangement imaginable, with the patient at the bottom of the pecking order knowing the least about what is going on. Many radiologists say, as Dr. McClenahan reports, "I am not going to tell the referring physician his patient is pregnant so he can reconsider the examination because I will be fired." Technologists say, "we are not going to tell the radiologist about mistakes and I am not using gonad shielding because poor quality X-ray films are thrown away because we will be fired."

People work under a lot of pressure. One of the difficulties in passing a law for certification is you can't get at these more subtle problems.

Mr. **Rogers**. What is the best way to get at it? Is it to try to have some public education for the public?

Dr. **Laws**. Fundamentally, I think I believe that it is an educational problem rather than a legislative problem because funding for educational projects on all levels will be much more effective than legislation. That is my opinion.

Ms. **Kushner**. I think in the role of public education, the media could do a great deal more—and I have that in my amplified statement—than any amount of legislation, particularly the popular mass media like comic books, soap operas. If somehow they could be encouraged to incorporate this information into their plots, it would reach a lot more women than the in-depth documentaries and articles in the Atlantic monthly, Harpers, and books. People just don't read them or watch those programs. It is sad, but true.

Mr. **Rogers**. Dr. Reiskin.

Dr. **Reiskin**. I think one of the mistakes we may make is tacitly assuming that physicians and dentists are flawless and perfect and, if given the correct information, they will inevitably do the right thing. I think they are as susceptible to pressure and to political influence and to economic as everybody else. But it is certain that if they don't know what they are doing, they can't do a good job of it. That is why I think it is so important to start with the education of the people who are involved in these procedures. If they don't know what they are doing, they are going to bungle it, and that is for certain.

They may bungle it anyway, but at least they have a chance to do the right thing if they have been properly educated.

I think legislation is a value not because it will insure that everybody does the right thing, but at least it will give some force to the people who want to do the right thing. Right now, the technician who wants to advise her physician that a patient is pregnant is afraid to do it because there is only a biological basis for raising that issue. I think legislation would help that kind of problem work itself out.

Mr. **Rogers**. Should X-ray machines be sold to persons who have not had courses in radiology and certified as having been trained in radiology?

Dr. **Phillips**. I don't really think they are now.

Mr. **Rogers**. I thought a dentist didn't necessarily have to have radiological training.

Dr. **Reiskin**. They don't have to have very much.

Mr. **Rogers**. Should you have a minimum amount?

Dr. **Rfiskin**. I think there should be a minimum amount, yes.

Mr. **Rogers**. What is your feeling?

Dr. **Phillips**. In the field of medicine, I believe that anybody who graduates from medical school now has had a minimum exposure, and I say a minimum exposure.

Mr. **Rogers**. That is not what I am getting at. Have they had an adequate amount so that a machine should be sold to them where they will operate and have responsibility for operating that machine?

Dr. **PHILLIPS**. I would say that this does not occur in medical education.

Mr. **ROGERS**. It does not now occur in medical education?

Dr. **PHILLIPS**. It does not now occur so that they should go out and buy a machine and put it to use.

Mr. **ROGERS**. Even though they are not really adequately trained to use the machine?

Dr. **PHILLIPS**. Yes, that's what I am saying; they are not adequately trained.

Mr. **ROGERS**. Do any of the courses get into the risks involved?

Dr. **PHILLIPS**. I think they have been paying more attention to risk in the last few years, but prior to that, I think the risks were neglected as far as instructing is concerned.

Mr. **ROGERS**. It is more how you take a good picture, isn't it?

Dr. **PHILLIPS**. Right.

Mr. **ROGERS**. But it is my understanding they have not gone into the problem much of risks, nor have we actually known what these risks are because maybe we haven't done sufficient research to get those results known.

Dr. **MCCLENAHAN**. Many of them don't know a good picture when they see one, unfortunately.

As has been indicated, a high percentage of films, when resurveyed, are found to be technically inadequate that were accepted at the time, that were interpreted at the time.

Mr. **ROGERS**. In other words, would you have any idea of what that might be?

Dr. **MCCLENAHAN**. I thought we heard the figure of 30 percent.

Dr. **REISKIN**. It was higher than that. It was closer to 60 percent.

Mr. **ROGERS**. About 60 percent?

Dr. **REISKIN**. About 60 percent were rejected. There was a study with Pennsylvania Blue Cross, and it was something close to 60 percent of the films that were rejected as inadequate to support the proposed treatment.

Mr. **ROGERS**. Given.

Dr. **REISKIN**. Poor films were submitted, and presumably were approved and accepted and used by the practitioner.

Ms. **KUSHNER**. May I point out my mammogram was a false negative. It said I have nothing to worry about. Go home and forget it.

Mr. **ROGERS**. Now, did you have another which did——

Ms. **KUSHNER**. No; I just decided not to listen. I had a symptom and I decided to have a biopsy, because that is the only way to know. A mammogram is not 100 percent either way; it is 85 percent, maximum. I was afraid I might be in that 15, and I was.

Dr. **LAWS**. When we talk about education, I think that the various people who are responsible for prescribing, reading, and conducting X-ray examinations need to learn different things about the process. Across the board, I think we need to have more education about risks. Dr. McClenahan talked about something very important, and that is having a medical student in any specialty, not just radiology, have a much better understanding of which kinds of symptoms might indicate that an X-ray diagnosis is useful and which symptoms lead to X-ray examinations which are just wild goose chases.

Mr. ROGERS. Has this been determined?

Dr. LAWS. Not completely for all examinations. Of course, the recent studies of skull X-rays provides an example of the dose reductions achievable with a better understanding of symptoms leading to a useful examination with X-rays. I think high yield criteria likewise associated with skull X-rays need to be developed for every common X-ray examination. It is expensive to develop these, but I think it would be worthwhile.

Mr. ROGERS. Would everyone agree to that?

Dr. MCCLENAHAN. It has not been determined, Mr. Rogers, because I think one deals in a gray area here in which clinical judgment is the most important consideration.

But if, for example, a patient falls and sprains an ankle and it hurts and it gets better and in 3 days he is well and in a week the doctor says, "You better go and have an X-ray," the chances are that it is not going to show a fracture. In that instance, the examination was done for a purpose other than a diagnosis and this, I think, is frequent.

The hard thing and the difficult thing to categorize is the importance of leaning more heavily on the eyes and the ears and the fingers rather than on the film.

Dr. LAWS. The only thing I need to comment about the high yield criteria, I am not advocating one develop these criteria for exams and then legislate that physicians must follow a formula, because we are talking about professional judgment. But if these criteria are developed and become part of the medical literature and part of the lore of the medical community, I think people will make better judgments.

Dr. REISKIN. I would like to add one comment. I think that high yield criteria becomes a greater necessity when one does not understand the mechanisms by which the image is produced, and I think if, in most instances, it were left to the judgment of the radiologist to determine what examination to do or whether or not to do it there wouldn't be a need for high yield criteria. The problem is that for the most part, the individual ordering the examination does not understand the capacity of the examination to give him a result. He is hostile when a radiologist tells him "I don't think you should do that." That is where the problem lies.

Mr. ROGERS. Could you comment on that?

Dr. MCCLENAHAN. Several years ago I attended a convention, a meeting in Tucson, the purpose of which was to determine when X-rays are of value in weeding out individuals who should not do heavy work. This conference was sponsored by orthopedists, radiologists, industrial physicians, and it was paid for by the Government.

We spent a week at Tucson discussing this. At the end of the discussion, a large report was printed. But, having been there, I was puzzled because at that time we didn't even decide what constituted an adequate X-ray examination of the low back, technically. We never got this figure.

Mr. ROGERS. So we need to develop some criteria.

Dr. MCCLENAHAN. Yes.

Mr. Rogers. And how it would be applied.

Dr. Bertell?

Dr. Bertell. There is another dimension to use, too. This has been on my mind since you asked the other question about what if the person is not able to operate the X-ray equipment, should you sell it to them.

I think by making equipment convenient in almost every doctor's office or something, to really push it in order to make it cost-effective, you use it. So, even though the person is competent, if it is a single office or something, I don't think we should have X-ray equipment on the basis that in order to make it cost-effective, they have to use it.

Do you know what I am trying to say here? I was involved in the purchase of a CAT scanner in Vermont, for example. Now, they paid a half a million dollars for that in a small State with CAT scanners available in Albany and in New Hampshire and in Quebec. I think we figured there was a CAT scanner within 50 miles of every person in the State of Vermont, and there was a need there for that half a million dollars besides putting it in. It was a matter of accreditation and prestige for the medical school, I think, at Burlington.

These other considerations have to be faced up to also. Maybe just localizing even the X-ray centers in some way and not making them quite so convenient would be a help.

Dr. Laws. I feel very torn by those recommendations. One approach to obtaining more competent personnel is to set up very sophisticated X-ray centers and not allow doctors to take X-rays in their own offices. But, we tend to have problems of communication in large sophisticated X-ray centers.

The other approach is to develop small X-ray facilities, like those in Dr. McClenahan's office, where a certified radiologist operates a private practice. In general I have more faith in small operations. However, many of the small X-ray facilities are run by nonradiologist physicians and dentists who are making money for themselves by ordering and taking lots of X-rays. This is called self-referral. We need to look for ways to keep small environments going without giving the physician or dentist an economic incentive to prescribe unnecessary X-ray examinations.

Mr. Rogers. Shouldn't medicare and medicaid really approve X-rays, or even Blue Cross, unless there has been an approval given by the radiologist of that procedure?

Ms. Kushner. A radiologist will always find someone to approve a procedure in his or her community.

Mr. Rogers. A radiologist?

Ms. Kushner. Someone ordering an X-ray can always find a radiologist to go along with him.

Mr. Rogers. I understand. But that is like a second opinion. And it has had some effect; second opinions. If there is a pattern of all of the X-rays going to one radiologist, then I think that would warrant the PSRO looking at the situation, and should the PSRO and third-party payers require the application, say, of high yield criteria, as they are developed.

Dr. **McClenahan.** I think a second opinion would be very useful, but I think it would be awkward and terribly difficult to administer.

Mr. **Rogers.** Here is what I was saying: Not a second opinion, but rather have the radiologist who is going to do the work anyhow make the judgment that that is appropriate, an appropriate procedure for the purpose.

Dr. **McClenahan.** I think it would be good if that were true, but I think it would be very often possible for him to rationalize the procedure.

Mr. **Rogers.** I am sure it would many times, but many times he might say: Well, I don't really think this is appropriate.

Dr. **McClenahan.** I think that would be a useful gambit for him.

Mr. **Rogers.** At least we would get something along these lines.

Thank you for being present today. We are sorry to have held you for so long, but your testimony has been most helpful for the committee. If you have additional suggestions, we will be pleased to receive them in writing. Thank you so much.

The committee stands adjourned until 2 o'clock tomorrow afternoon.

Thank you.

[The following materials were received for the record:]

RESPONSES TO QUESTIONS ON MEDICAL AND DENTAL DIAGNOSTIC X-RAY

By Rosalie Bertell

A. Risks to Human Health.

1. I have been responsible for some of the new findings on the effects of low level ionizing radiation. On the basis of my own research experience, and my familiarity with the findings of others, I believe that the effects have been seriously underestimated in the past. I also believe that the methodology for measuring a hazard with such broad based health effects has been a part of the problem. In this testimony and elsewhere, I have proposed using natural aging as a yardstick. It is time that the Nuclear Regulatory Commission and the BEIR committee took this proposal seriously.

   Methodology: Presented at the 9th annual International Biometric Conference, August 1976

   Findings: Presented at the National meeting of the Americal Public Health Association, Nov. 1975.

   Published: "X-ray Exposure and Premature Aging", Journal of Surgical Oncology, August 1977.

2. The problem is much broader than medical/dental use of X-ray. The population of the United States has been subjected to serious radioactive pollution from weapons production and testing, from uranium mining and careless disposal of mine tailings, and from management of the fuel cycle for nuclear generators and nuclear waste disposal. As a result of the nuclear industry, new medical uses of radio-nuclides have been discovered, and new technology developed. We have witnessed an introduction of new scanning techniques, computerized axial tomography, mammography, panalapse, etc. Much of this increased medical use of radiation has fed a public relations image of radiation as not only "harmless" but even beneficial. The trend of reducing radiation exposures, which was seen since 1900, has seemingly been reversed, and the medical community now seems to be following the advise of the military-industrial complex.

BEST COPY AVAILABLE

In calling for greater responsibility among health professionals in the use of X-ray, I am also calling for a restoration of leadership in matters pertaining to the public health, to the health professionals.

I would like to add three conditions to my answer. Without attention to these things, I believe that a government campaign against excessive medical or dental use of X-ray would be counter-productive.

1. It should never happen, nor an impression be given, that individual quality medical care is sacrificed so that background radiation may be increased through weapons production or nuclear generation of electricity.

2. A sophisticated public health monitoring system capable of acting as a check on sophisticated technology must be immediately implemented. At present the public has neither legal evidence nor an early warning mechanism for deteriorating public health situations due to environmental pollution.

3. The federal guidelines for radiation should be reviewed in open hearings. Those who speak for reducing the exposure limits should not be handicapped by lack of resources and/or funding.

While it is easy to point the finger at medical X-ray because of the high individual doses received from this source, it must also be recognized that such exposure brings direct benefit to the recipient, and is knowingly received. There is some ability to refuse and/or control this source. When one is dealing with radioactive material added to the air, water and food chain, there is no awareness of being exposed or ability to refuse or protect oneself from the hazard. The human body cannot distinguish between radioactive nuclides and their non-radioactive chemical counterparts. It will incorporate this material into the bone and tissue of the body. Without legal and social protections, this hazard poses a much greater public health problem, in my opinion.

3. I would recommend that patients cumulative records of X-ray exposure be kept, and that no more than one trunk equivalent* every two years be permitted on the average. This would, of course, exclude an emergency situation. Signing of an X-ray order by two physicians or dentists, and the patient (or guardian), and a signed record of the number of plates used by the X-ray technician should be manditory. Routine X-ray or screening of asymptomatic persons should be illegal. Lead apron should be used if possible.

* One trunk X-ray, or four non-trunk X-ray.

B. 1. If X-ray procedures means examinations, then 30% seems about right. If you are talking about X-ray plates used, I think 50 to 70% could be eliminated without lowering the quality of medical care. It involves eliminating unnecessary duplication, and elimination of X-ray when further knowledge cannot result in better medical care.

2. I am not qualified to answer this question. It is a matter of equipment inspection, and medical determination of necessity. I would consider any X-ray taken to protect against mal-practice suits, to make equipment cost efficient or for purely informational purposes to be unnecessary.

3. (a) Factors influencing unnecessary X-rays:
   - Failure to educate physicians and dentists to this hazard;
   - Patient demands through ignorance of the hazard;
   - Propaganda from the nuclear industry and the Dept. of Energy;
   - Desire to make X-ray equipment available in every office, followed by the necessity of then making it cost efficient;
   - Automatic pass-on of costs to insurance companies or government programs.

   (b) Factors influencing unnecessarily high exposures:
   - Faulty or outdated equipment;
   - Lack of inspection of equipment;
   - Untrained/ unlicensed X-ray technicians;
   - Optimizing diagnosis beyond the ability to treat disease.

4. There are few, if any, incentives for cutback on diagnostic X-ray. These medical procedures are well below the threshhold for immediate radiation sickness reactions. Damage is usually undetectable by either doctor or patient for several years, at which time there is little likelihood of association with the exposure. Unfortunately, the use of modern radiation equipment and nuclear medicine enhances the physicians mystique of being modern and thorough. There are little or no economic barriers to act as deterrents.

5. In the light of present research, educational programs in general, and medical educational programs in particular, are totally inadequate for the protection of the public health relative to exposures to ionizing radiation. Few physicians or dentists are able to keep up with research journals.Many are still believing the myth that "sitting out in the sun for an hour exposes one to more radiation than this X-ray". An average dental examination gives roughly 2000 times the ionizing radiation exposure as one hour exposure to cosmic radiation!

C. Recommendations for reducing exposures of the population from unnecessary diagnostic radiation:

Drastic changes in attitude are needed, and this will have to begin with education - both medical and general.

Perhaps written authorization for X-ray by two attending physicians, and written consent of the patient (or guardian) might help. Notification of physicians relative to the number of radiologic examinations ordered, and the average number ordered by physicians in the same specialty might help. All of these functions could be performed by the insurance agency without interfering with medical care.

Guidelines, as for example those recently drawn up for mammography or for gonadal exposure, are often ignored. Tying federal funding with observing of the guidelines might help. Convincing the doctors is still the most important goal.

Improvement of techniques which would minimize exposures should be on-going, and implemented as soon as possible. Government assistance to clinics which serve the poor would be in order.

Education of the public is most important!

Routine screening programs and pre-admission X-rays for hospitals and some employment should be eliminated.

I have been asking for and receiving medical and dental X-rays for several years now. It causes surprise when you ask, but I have yet to be refused.

Complete patient records of all X-ray exposures should be kept by the patient, attending physician and dentist.

(2) This is a question for the doctors to answer. I would say though, that I remember when diagnosis was an art, and patient-doctor communication was more important than technology. Obviously, I am not opposed to all uses of technology for diagnosis!

(3) This is not my expertise.

(4) (a) My experience with X-ray technicians has been that the most intelligent and careful ones are also the most knowledgeable about the hazards. Often they are inwardly in conflict with radiological policies in the lab where they are working. This tension must cease, or these well qualified technicians will not continue in the field. They are needed!

4. (b) Better selection and training of technicians would be an obvious help. I believe that technicians should also be licensed. They also need the support of the radiologist in their efforts to eliminate unnecessary X-rays and exposures.

   (c) Ultimate responsibility belongs to the physician in charge of the X-ray laboratory.

   (d) They bear the responsibility for reducing exposures of the patient and of the X-ray personnel to an absolute minimum.

5. (a) This in not my area of expertise.

   (b) I think the U.S. Public Health Service should assume this responsibility. I would like to see this agency acting much more decisively on behalf of the public health. Its focus should now be on environmental health problems.

   (c) I don't believe so.

   (d) Restore funding of the Tri-State Leukemia Survey analysis and guarantee a broadly based research team to review the analysis and recommendations.

   (e) Perhaps there is some way to protect scientists who speak contrary to the wishes of big business, big medicine and big government. The corruption of science has become so bad that when one tries to report findings, one is immediately labeled as pro or con some political position. It should be possible for a scientist to report findings, and let the chips fall where they may!

6. (a) The medical profession is now sole arbitor of patient exposure to diagnostic X-ray. This role needs to be modified partly by informational input (to counteract technological P.R. materials) and partly by enforceable guidelines. Patient education will also help.

   (b) I see the State regulatory role as important in monitoring equipment and licensing of X-ray technicians. I would also like to see modernizing of Public Health statistics routinely gathered. Present information flow is geared to solving the problems of the past - infectious diseases - and not the present - environmental diseases.

   (c) Informational feedback.

   (d) I believe in a check and balance type of control.

There have been fundamental changes in public health problems in the last thirty years, without a change in the check and balance system. Our public health problems are chronic diseases, and the primary causes of these diseases are environmental. Until we change the focus of our public health services and information collection to meet this new situation we will be in trouble. There is no need for the present confusion about saccharine, PCB,PBB, mirex, kepone, asbestose, radiation and other hazards. There is also no need to mount a separate governmental study to deal with each one!

I would like to see the Federal government take leadership in evolving an effective Public Health Service, which would be a proto-type in the world, for the detection of environmental disease. There is strong backing for this proposal in a special report issued by the Technical Consultant Panel to the U.S. National Committee on Vital and Health Statistics (DHEW Publ.No.HRA 77-1457). I have also prepared a paper on the subject, and hope to see the plan implemented soon.

7. I see the role of the Federal government as providing for a check and balance with respect to all environmental health problems, as mentioned in 6.(d). It also has the obligation of protecting the public from excessive claims of those who promote technology. This is probably best done when there is free flow of scientific information, scrutiny of funding practices, and some advocacy procedure available to scientists which would provide meaningful scientific debate and protection of the scientist from economic coersion.

I would not like to see the Federal government handle the problem of medical X-ray in isolation from the bigger problem of environmental diseases. We have already seen that efforts to prevent X-ray exposure of pregnant women led to an introduction of ultrasound examinations - with absolutely no guarantee that this technology would be any better!

Dr Rosalie Bertell

THE UNIVERSITY OF CONNECTICUT
HEALTH CENTER

November 1, 1978

The Honorable Paul G. Rogers
Chairman, Subcommittee on Health and
the Environment of the Committee on
Interstate and Foreign Commerce
Raybury House Office Building
Room 2415
Washington, D.C. 20515

Dear Sir,

At the oversight hearings on medical and dental diagnostic x-rays which were held on July 11-13, 1978, the Subcommittee asked witnesses to comment on several issues including the need for legislation to prevent the sale of x-ray machines to unqualified users and the desirability of establishing minimum educational requirements. My apologies for not responding more quickly. It has taken some time to accumulate data and I also wished to review material which was submitted to your committee in response to my testimony.

I have contacted several colleagues who hold teaching or administrative positions in medical schools and I have not been able to uncover any specific requirements for education in radiology. It was the opinion of several individuals that most medical students receive basic instruction in radiographic interpretation during the course of their medical education but the background of medical students in radiation physics, radiation biology and x-ray technology appears to be extremely variable and may be nonexistent in some institutions.

In dental schools the situation is not dramatically different with the exception that x-ray diagnosis is usually taught be individuals who themselves lack expertise (see the testimony of Dr. Robert Goepp). As in medical schools, there is no specific requirement for a minimum educational experience for undergraduate dental students. As noted in the testimony of Dr. Harry Bruce, representing the American Association of Dental Schools, the Association provides dental schools with guidelines, with the following qualification: "They are not official policy statements of the AADS and should not be construed as recommendations for restrictive requirements". The recommendations to which Dr. Bruce referred were offered as the basic minimum and as Dr. Bruce's testimony indicated, there are many dental schools which fail to meet the recommendations included in the dental radiology teacher's manual. In point of fact, I have never been asked about our educational program or clinical practices by the AADS or by the American Dental Association's accreditation committees. It is entirely possible that individuals could graduate from either medical schools or dental schools without an adequate basic education and therefore, there is reason to believe that the sale of x-ray equipment to unqualified users should be restricted. Even Dr. Bruce indicated that the cause of overexposure and overuse was related at least in part to the lack of controls.

It may also be of interest to the Committee to appreciate that the record statement of the American Association of Dental Schools on the oversight hearings focused primarily on my testimony and consistently referred to the data which I presented as being personal opinion, although the bulk of my testimony was documented by citations from the dental literature. Dr. Bruce neglected to provide any specific rebuttal beyond general statements indicating that the situation was improving. The generalizations which were cited as a justification for the extensive use of radiography in dentistry are poorly supported.

Overall, the response of Dr. Bruce to my testimony only reinforces my impression that as professionals we are guilty of benign neglect and will require external pressure or direct control to affect meaningful improvements.

My thanks for the opportunity to participate in the hearings. If I can be of further assistance, please contact me.

Sincerely,

Allan B. Reiskin, D.D.S., D.Phil.
Professor
Division of Oral Radiology

[Whereupon, at 5:25 p.m., the subcommittee was adjourned, to reconvene at 2 p.m., Wednesday, July 12, 1978.]

EFFECT OF RADIATION ON HUMAN HEALTH

Radiation Health Effects of Medical and Diagnostic X-Rays

WEDNESDAY, JULY 12, 1978

House of Representatives,
Subcommittee on Health and the Environment,
Committee on Interstate and Foreign Commerce,
Washington, D.C.

The subcommittee met, pursuant to notice, at 2:20 p.m., in room 2322 Rayburn House Office Building, Hon. Paul G. Rogers, chairman, presiding.

Mr. Rogers. The subcommittee will come to order please. Today the committee will hear testimony from the Food and Drug Administration and its Bureau of Radiological Health. We hope to outline and examine what the Administration has accomplished and what it is contemplating in carrying out the mission this committee assigned it in 1968 under the Radiation Control for Health and Safety Act of that year.

As we approached hearings on the issue of radiation as it affects health, we came to realize that although radiation in the generic has long been the subject of concern among medical and scientific minds and of this committee, the Federal Government has not responded to this concern.

Growing evidence indicates increasing cause for concern. Yet we find fragmentation of effort and philosophy among the Federal agencies and departments responsible for various parts of the radiation field.

For that reason, I do not think we can say that FDA is the lead agency in our Nation's effort to better understand and thus solve the problems facing us. I think there is no lead agency or department in radiation protection, and that is one of the problems.

Additionally, I do not see evidence that FDA, given a somewhat limited jurisdiction, has established a priority in the area of radiation protection. Concerns which have been voiced by men and women of science over radiation are not new ones. Papers have been published outlining data which should have sparked action years ago.

Yet, I do not see any evidence that this information has stirred the agencies to take necessary and appropriate action. The actual law was passed in 1968, but FDA did not promulgate standards until 6 years later. I realize that is before the current administration.

Data is still scarce. Public and professional awareness has not been properly promoted. Each inquiry into the lethargic behavior of the BRH has been met with the same answer: A lack of funds and manpower, and it appears that no effort has been made to remedy this situation.

The subcommittee hopes to be able to explore these issues in greater detail today.

We are pleased to have as a witness today Dr. Donald Kennedy, who is the Commissioner of Food and Drugs; Mr. John Villforth, who is Director of the Bureau of Radiological Health; and of course, Mr. Rich Cooper, who is Chief Counsel for the Food and Drug Administration.

We welcome each of you to the committee. We are appreciative of your presence here today. Your statement will be made a part of the record.

You may proceed as you desire.

STATEMENT OF DONALD KENNEDY, PH. D., COMMISSIONER, FOOD AND DRUG ADMINISTRATION, PUBLIC HEALTH SERVICE, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE, ACCOMPANIED BY JOHN C. VILLFORTH, DIRECTOR, BUREAU OF RADIOLOGICAL HEALTH; AND RICHARD M. COOPER, CHIEF COUNSEL

Dr. KENNEDY. I thank you very much, Mr. Chairman. Each time I hear some reference to my agency's past and then that polite little apology that that was before I came, I have this acute sense that the time at which I will enjoy that special protection is ebbing rapidly away.

Mr. ROGERS. Mr. Commissioner, you have stated it correctly.

Dr. KENNEDY. In the 10 years since you set in motion the events that led to the enactment of Public Law 90-602, the Radiation Control for Health and Safety Act of 1968, FDA has made significant progress, we think, in developing a nationwide program to protect the public health and safety from dangers of exposure to various forms of electronic product radiation.

It is a pleasant task, not only to acknowledge your foresight but to express our appreciation for the essential role you played in the establishment of this radiation protection program. I think my obligation here this afternoon and that of my colleagues is to tell you how we are using Public Law 90-602 to accomplish the goals envisioned for it for medical radiation and how we are using it to make a difference in the health care of the Nation.

Mr. ROGERS. May I interrupt just to say this: The law then passed zeroed in more, as you may recall, on the TV problem, and the microwave oven problem. This oversight hearing, hopefully, will point up those areas where the law may need to be strengthened, and we realize it does, to perhaps give more authority to zero in on deficiencies in the current law.

So we would hope that you could also give advice to the committee on those areas where you think we need to strengthen the law.

Dr. KENNEDY. We will try to do that, Mr. Chairman, at the end.

I would like to begin by pointing out that over the last decade, products that emit radiation have proliferated considerably, and so the potential for exposure has increased.

Let me just briefly sketch the universe of medical and dental X-ray exposure we face today. About 145,000 dental X-ray machines are being used in 84 million procedures yearly, and about 125,000 medical X-ray machines in about 157 million procedures. Of the 270,000 instruments in use, 19 percent are complete X-ray systems manufactured and sold after August 1, 1978, the effective date of FDA's performance standard.

These are certified instruments. About two-third of medical X-ray examinations occur in hospitals, with the remainder taking place in physicians' offices, group practices, health agencies and the like. Between 110,000 and 170,000 persons operate medical X-ray equipment in the U.S., of whom approximately 80,000 are certified or licensed to practice.

There is some evidence that the actual exposure people are receiving from medical sources may also be on the increase, simply because of the increased number of medical radiologic procedures now being performed.

For example, two FDA-conducted national surveys of X-ray use showed that the annual number of X-ray examinations in the United States increased 24 percent between 1964 and 1970 from 173 million to 212 million. The cost of these household-based surveys has made it prohibitive to continue them, but we can derive a rough estimate of today's usage by extrapolating from those 2 years. When we do that, we come up with a figure of about 241 million examinations which would have been performed last year.

A further increase in the overall number of radiologic examinations, possibly in the average radiation exposure as well, may be witnessed as a result of the introduction of computed tomography scanners in the United States. Already about 780 such machines are being used on about 2 million patients per year.

Mammography has also contributed to increased exposure over a short period. This procedure, in which relatively large amounts of radiation are delivered to a particularly radiosensitive tissue, was scarcely used as recently as 15 years ago, but it is now being performed on about 2 million women in the United States annually.

From here on, Mr. Chairman, I am going to summarize what is a long statement by just touching on the main elements of the sections, hoping that you and your colleagues on the subcommittee will turn my attention back to them by your questions.

Our program is divided into six functional components that I am going to discuss here. First, biological effects research; second, radiation measurement research; third, regulatory performance standards and their development; fourth, recommendations on what is good practice; fifth, professional and public education; and sixth, cooperative programs with the States.

I will be submitting for the record, Mr. Chairman, a summary look at FDA's programs to protect the American consumer from radiation.

Mr. ROGERS. Without objection, it will be made a part of the record.

[Testimony resumes on p. 221.]

[The following information was received for the record:]

HEW Publication (FDA) 77-8032

THE
BUREAU OF RADIOLOGICAL HEALTH

A Look at FDA's Program to Protect the American Consumer from Radiation

April 1977

BRH
bureau of radiological health

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
Food and Drug Administration

FOREWORD

The Food and Drug Administration's Bureau of Radiological Health conducts a nationwide program designed to limit man's exposure to ionizing and nonionizing radiation. To this end, the FDA: (1) develops criteria, standards, and recommendations for safe radiologic practices; (2) develops methods and techniques for controlling radiation exposure; (3) plans and conducts research to determine health effects of radiation exposure; (4) provides technical assistance to agencies responsible for radiological health programs; and (5) conducts an educational program to improve the practices of those who use radiation.

This report provides a brief overview of the FDA's major regulatory and voluntary efforts in the area of radiation control, and examines the impact of the Agency's programs to eliminate unproductive radiation exposure to the American consumer. It concludes with a summary of present and future concerns about newly-emerging radiation-emitting products and uses, and the potential public health problems which they may engender.

Readers are encouraged to report errors or omissions to the Bureau of Radiological Health. Comments or requests for further information are also solicited.

John C Villforth

John C. Villforth
Director
Bureau of Radiological Health

CONTENTS AND SUMMARY

Page

I. What is the overall mission of the FDA's Bureau of Radiological Health? 1

Functions include monitoring radiation exposure of population from medical and consumer products; assessing the public health risks involved; and conducting action programs to reduce unnecessary or unproductive exposure. This is mandated in part by P.L. 90-602, the Radiation Control for Health and Safety Act of 1968 (an amendment to the Public Health Service Act), which authorizes the HEW Secretary to establish performance standards for radiation-emitting electronic products, carry out research and training, and make recommendations necessary to reduce risks to the public. Further authority is contained in other parts of the Public Health Service Act, and the Food, Drug, and Cosmetic Act.

II. Why are public health authorities concerned about exposure of the population to radiation? 1

Exposure to radiation may result in biological injury. At high radiation doses, this injury generally gives rise to immediate and dramatic effects; e.g., skin burns from ultraviolet light or radiation sickness from large amounts of x rays. Low doses of radiation, which may be received by large segments of the population, have more subtle and insidious effects which often take many years to show up. They are generally measured by demonstrating a statistical increase in a chronic disease (e.g., cancer) among people who have been irradiated, as compared with those who have not. The long-term biological effects of some of the more recently used forms of radiation, such as microwaves and ultrasound, are still unclear and are cause for concern.

III. Are people being exposed to more radiation now than in the past? 2

Potential exposure is greater because of an increasing number of radiation-emitting consumer products, such as color TV and microwave ovens. Second, actual exposure from medical radiologic procedures is on the increase; these procedures include both conventional diagnostic techniques and newer modalities such as computed tomography (CT) scanning and mammography.

Page

IV. What is the FDA's strategy for minimizing exposure? 3

For consumer products, the goal is to eliminate any significant exposure of the user through mandatory performance standards, which insure adequate design and manufacturing safeguards. For medical products, which deliver radiation to the patient purposefully, voluntary recommendations and educational programs are developed to improve the radiation practices of medical personnel, and mandatory performance standards are established for medical radiation equipment.

V. What are the results of FDA's efforts to date with medical and dental products? What will be the results of new initiatives? 4

REGARDING EQUIPMENT PERFORMANCE...

A. Patients are being exposed to less unnecessary radiation from diagnostic x-ray machines as a result of FDA's performance standard for diagnostic x-ray equipment. 4

B. Dental patients and personnel are no longer risking burns from faulty ultraviolet plastic-hardening devices because of FDA's declaration of product defect and subsequent corrective action by the manufacturer. 5

C. Medical diathermy equipment will be more reliable as a result of FDA's proposed ultrasonic therapy and surgery equipment performance standard. 5

D. State regulations for the control of radiation are more consistent and compatible because of FDA's coordination of Suggested State Regulations for Control of Radiation, now adopted by over 40 States. 6

REGARDING JUDGMENT IN ORDERING EXAMINATIONS...

A. Medical students and practicing physicians are receiving better training in good radiation practices with the help of an FDA-produced learning system. 6

B. More is known about the quantitative risks of certain x-ray procedures, such as mammography, because of FDA's studies on risk/benefit problems. 7

C. Women and their physicians are becoming more aware of the problems associated with x-ray exposure during pregnancy because of FDA educational programs. 7

Page

REGARDING TECHNIQUES IN PERFORMING EXAMINATIONS...

A. Dental patients are receiving less unnecessary x-ray exposure because of improved quality control produced by an FDA-designed action program now being carried out in 37 State and local jurisdictions. 8

B. Women receiving mammography will be assured of receiving minimum radiation to the breast because of an FDA-developed corrective action program to be implemented by State and local health agencies. 8

C. Better quality assurance procedures in medical facilities will result in less radiation exposure and better x-ray diagnoses because of FDA's recommendations in this area. 9

D. X-ray technologists are receiving improved training in protecting their patients as a result of FDA-developed training materials which are widely used in technology schools and hospitals. 9

E. The general population will be receiving less exposure of the reproductive organs because of better utilization of gonad shielding as a result of the Agency's shielding recommendation and its associated educational campaigns. 10

F. A safer form of radioactive iodine is now available for medical use because of FDA research and development initiatives. 10

G. Patients receiving radiation therapy will be assured of accurate dosage due to the Agency's proposed actions on therapy equipment used in the treatment of cancer. 11

VI. **What are the results of FDA's efforts with consumer products?** 11

A. Viewers of color television need no longer be concerned about x-ray exposure because of FDA's performance standard and its associated compliance program, which has discovered and corrected nearly half a million noncompliant TV sets. 11

B. Owners of microwave ovens are no longer exposed to hazardous levels of radiation due to the FDA performance standard for these products. 12

C. Airline personnel and passengers are not being exposed to x rays from baggage inspection systems because of the Agency's performance standard, which affects 144 U.S. airports. 13

Page

D. Laser devices are being better designed for safety as a result of the FDA performance standard. 14

E. People will not risk eye damage from mercury vapor lamps because of a performance standard which is being developed for this type of product. 14

F. The risk of injury from sunlamps will be reduced because of a proposed performance standard which will affect the approximately one million of these products sold annually. 15

VII. What concerns us about the future? 15

A. Uncertainty regarding the indications for medical radiation procedures 15

Some unnecessary exposure is due to the ordering of unnecessary radiologic examinations. Part of the problem is a lack of scientific criteria for physicians on when these examinations are indicated. This calls for the Agency's attention in the future.

B. The effects of new technology 16

As new developments and applications are designed, FDA must assure public safety, through: (1) developing new radiation measurement techniques; (2) revising existing standards or developing new ones; and (3) selectively promoting those new developments which contribute to lowered population exposure. Examples of new technological developments which FDA must deal with are rare earth x-ray screens and computed tomography (CT) scanners.

C. Concerns about the biological consequences of exposure 17

In order to assure effective protection programs, more information is needed about the health effects of radiation. For example, for some of the more newly used forms of radiation, such as diagnostic ultrasound, the extent of the risk, if any, is still not known with certainty. The carcinogenic potential of certain existing diagnostic and therapeutic radiation procedures needs further clarification. Certain types of radiation which have been used for many years, like radio-frequency radiation, may pose a hazard as yet undefined.

VIII. Where to from here? 18

FDA's Bureau of Radiological Health has two responsibilities, now and in the future. The first is to continue to assure compliance with present regulatory standards and to promote widespread adoption of existing voluntary recommendations. The second is to keep abreast of evolving technology and its associated biological risks, and to shape our programs accordingly.

THE BUREAU OF RADIOLOGICAL HEALTH

A Look At FDA's Program To Protect the American Consumer From Radiation

I. WHAT IS THE OVERALL MISSION OF THE FDA'S BUREAU OF RADIOLOGICAL HEALTH?

The FDA's functions include monitoring the radiation exposure of the population from a variety of sources, including medical and consumer products; assessing the public health risks involved; and conducting action programs to reduce exposure that is unnecessary or unproductive.

This mission is mandated in part by P.L. 90-602, the Radiation Control for Health and Safety Act of 1968 (an amendment to the Public Health Service Act) which authorizes the HEW Secretary to establish performance standards for radiation-emitting electronic products and to carry out research and training for the "protection of public health and safety." In the words of the Act, the Secretary is required to "develop and administer product performance standards," "plan, conduct, coordinate, and support research, development, training, and operational activities to minimize emissions of and exposure of people to, unnecessary electronic product radiation," "maintain liaison with and receive information from other Federal and State departments...," "develop, test, and evaluate the effectiveness of procedures and techniques for minimizing exposure to electronic product radiation," and "make...recommendations relating to...hazards and control..."

Further general statutory authority for the Agency's activities is provided in other parts of the Public Health Service Act, which enables the Service to conduct research, educational programs and cooperative Federal-State projects, and in the Food, Drug, and Cosmetic Act.

II. WHY ARE PUBLIC HEALTH AUTHORITIES CONCERNED ABOUT EXPOSURE OF THE POPULATION TO RADIATION?

Simply stated, the net result of human exposure to a wide variety of radiations often is biological injury. At high radiation dose levels, this injury generally gives rise to immediate and dramatic effects, such as the skin burns that result from ultraviolet light or the radiation sickness caused by large amounts of x rays. Low doses of radiation are characterized by more subtle and insidious effects that often take many years to show up. They are generally measured by demonstrating a statistical increase in various chronic diseases among people who have been irradiated, as compared with those who have not. Examples of these long-term or delayed effects include an increased incidence of various kinds of cancer as a result of exposure to x rays and radioactive materials. The greater the number of people exposed to low-level radiation...whether from industrial applications, consumer products or medical sources...the greater the number who will suffer the long-term consequences.

To add to our concern, the biological effects of some of the newer (and widely used) forms of radiation are still unclear. For example, it is known that high exposures to ultrasound, as might be used in medical diathermy treatments, result in measurable tissue changes, but the biological results of smaller exposures...from diagnostic medical ultrasound, for example... are not yet clear. The same situation pertains to microwave exposure; large amounts result in clearly measurable damage, while the effects of smaller exposures are still debatable.

Another troubling unknown is the possible synergistic effect between radiation and other cancer-causing materials such as industrial pollutants, drugs or chemicals in man's environment. It is possible that individuals exposed to more than one carcinogenic agent will be subjected to an increased cancer risk which exceeds that from any one of the individual agents.

III. ARE PEOPLE BEING EXPOSED TO MORE RADIATION NOW THAN IN THE PAST?

Because of the advent of a greater and greater number of consumer products that emit radiation...and spare the user from hazardous radiation exposure only by virtue of adequate design...the potential for exposure from consumer products has increased. With respect to medical radiation, where human exposure is necessary to achieve the desired result, actual exposure may also be on the increase simply because of the greater number of medical radiologic procedures being performed. FDA radiation control efforts are designed to keep this exposure to a minimum commensurate with the medical benefits which accrue from it.

Usage figures are dramatic. For example, approximately 13 million color television sets, that can emit x radiation without proper design safeguards, are now manufactured annually for the U.S. market. The increased sale of microwave ovens has led to the prediction that 11 million ovens...each potentially capable of exposing the user to substantial amounts of microwave radiation unless designed and manufactured properly...will be in use in this country by 1980. The list grows, with 477 x-ray baggage systems now operating in one-third of major U.S. airports, and annual sales of ultraviolet-emitting sunlamps now approaching the 1 million mark. In the medical field, the number of x-ray examinations has risen steeply in recent years. Between 1964 and 1970, the annual number of examinations in the United States had increased 24 percent, from 173 million to 212 million. An extrapolation of this data shows that approximately 270 million examinations will be performed in 1977. A similar rise has taken place in nuclear medicine, in which radioactive materials are used to diagnose diseases. Between 1971 and 1973, these procedures increased by 55 percent.

With the recent advent and proliferation of x-ray computed tomography (CT) scanners, we can expect an even sharper increase to take place in the number of examinations performed, and possibly also in the average radiation exposure per examination. Already, approximately 400 CT scanners are being used on about 100,000 patients per year, and it has been projected that seven times this number of machines and patients will be reached in the years to come.

Sometimes a specific diagnostic x-ray procedure can undergo a rapid increase in utilization over a short period of time. This is the case with mammography (x-ray examination of the breast), which is used for the early detection of breast cancer. This procedure, in which relatively large amounts of radiation are delivered to a particularly radiosensitive tissue, was scarcely used as recently as 15 years ago. It is now being performed on approximately 2 million U.S. women annually, and health authorities are increasingly concerned about balancing the benefit of x-ray cancer detection against the risk of inducing cancers from the radiation.

Experience with the delayed consequences of past medical radiation reinforces our concern. In the 1930's through the mid-1950's, x-ray treatments, then believed harmless, were used for a wide variety of benign conditions, from acne to tonsillitis. Today, patients who received this therapy as children are being advised to have periodic thyroid checkups, since it has become clear that the risk of thyroid cancer is significantly increased as a result of the radiation treatment. A study of individuals who received x-ray treatments of the scalp, (tinea capitis) resulted in similar findings.

IV. WHAT IS THE FDA'S STRATEGY FOR MINIMIZING EXPOSURE?

The radiation-emitting products which pose a risk to public health and with which the Agency is concerned fall primarily into two general categories: (1) medical and dental products, such as x-ray machines, diathermy (heat producing) treatment devices and diagnostic ultrasound devices; and (2) consumer products such as color television sets and microwave ovens, as well as commercial products not used directly by consumers, such as airport x-ray baggage inspection systems, and certain industrial sources such as laser devices.

These two classes of products call for different strategies to minimize exposure. In the case of consumer products in which human exposure to radiation is only incidental to the intended use (e.g., the television set or microwave oven), the goal is essentially to eliminate any significant exposure by means of design and manufacturing safeguards. These are generally promulgated through regulatory performance standards that severely limit the amount of radiation a user could receive.

The situation is more complex with respect to radiation-emitting devices used in medicine, where the exposure of the patient is the desired outcome of the diagnostic or therapeutic procedure. In this instance the Agency has several concomitant goals. The first is to help assure that radiologic procedures are ordered by physicians or dentists only when they are clinically needed. This is accomplished through the development of voluntary recommendations on good radiologic practices, and the education of practitioners who prescribe radiologic examinations. The second goal is to help assure that once a radiologic procedure is prescribed it will be carried out with a minimum of radiation exposure to the patient. This is accomplished by means of regulatory performance standards for the manufacture of medical radiation equipment, and through educational programs for radiologists and medical radiation technologists. To complement these educational efforts for health care personnel, the FDA also educates consumers on how to help minimize their own exposure to radiation.

It should be noted that although the Radiation Control for Health and Safety Act requires the HEW Secretary to set standards for radiation-emitting electronic products, it does not provide for legal sanctions against improper use of this equipment. Thus the FDA's programs to improve radiation usage practices must be voluntary in nature, relying on the education of practitioners and auxiliary personnel.

V. WHAT ARE THE RESULTS OF FDA'S EFFORTS TO DATE WITH MEDICAL AND DENTAL PRODUCTS? WHAT WILL BE THE RESULTS OF NEW INITIATIVES?

REGARDING EQUIPMENT PERFORMANCE...

A. Patients are being exposed to less unnecessary radiation exposure from diagnostic x-ray machines.

One source of needless radiation exposure of patients during x-ray examinations is x-ray equipment that performs inconsistently. In addition, if the operator of the x-ray machine does not adjust the size of the x-ray beam to the size of the film or smaller, parts of the patient's body outside the area of clinical interest (including radiosensitive organs such as the reproductive organs and the thyroid gland) may be unnecessarily exposed.

To address this problem, the FDA promulgated the Federal Performance Standard for Diagnostic X-Ray Equipment in August 1974. The standard, which applies to all general purpose x-ray machines manufactured after that date, insures that the radiation output of x-ray equipment is consistent, that it is installed properly, and that those who use the machines receive adequate information about operation and maintenance. In addition, the standard requires machines to either automatically adjust the beam size before an exposure can be made, or to be inoperable until the x-ray technologist manually makes the proper adjustment.

For x-ray machines sold in 1976, the saving in future health care costs as a result of the lowered radiation exposure produced by the standard is estimated to be in excess of $70 million. This cost savings results primarily from the provision in the x-ray standard just discussed which is concerned with the limitation of the x-ray beam to the size of the x-ray film, thereby eliminating unproductive radiation exposure which would increase the potential health hazard.

B. Dental patients and personnel are no longer risking burns from faulty ultraviolet plastic-hardening devices.

Approximately 25 percent of practicing U.S. dentists are using a device that produces ultraviolet radiation to harden plastic materials used in the restoration of teeth. The longer wavelength ultraviolet light from the device is necessary to harden the plastic material, but the shorter wavelength ultraviolet radiation is not necessary and can be hazardous. A properly designed device, therefore, provides filtration to remove this unnecessary radiation.

Alerted by over 200 reports of skin and eye burns among dentists and patients, the Agency found that one model of this device, the Nuva-Lite, was producing short wavelength ultraviolet leakage radiation. Based on these injuries, a defect was declared on this product under provisions of P.L. 90-602. The manufacturer was required to conduct an extensive retrofit program of all the devices in use by the dental profession. The corrective action enabled 120,000 dentists to safely continue the use of a dental restoration process.

C. Medical diathermy equipment will be more reliable.

Ultrasound, a form of energy similar to but higher in frequency than ordinary sound waves, is used by physicians and physical therapists for "deep heating" treatments to relieve pain and promote healing in muscles and joints. Similar therapeutic effects are obtained with microwave therapy (diathermy) devices that also produce such heating effects. Approximately 15,000 medical microwave diathermy units are in use, delivering about 50 million treatments per year to 7 million patients. Millions of patients are also treated each year with ultrasonic therapy equipment. The radiation output of these units is inconsistent and not readily measurable by the operator. Some of these machines cannot deliver enough radiation for adequate treatment while others produce too much, resulting in injury to sensitive tissues.

The FDA has issued a proposed ultrasonic therapy performance standard, which would require that these devices deliver a prescribed amount of ultrasonic energy to the patient, and that sufficient information on radiation output be supplied to allow medical personnel to make informed judgments regarding safe and proper use. A similar standard for microwave diathermy equipment is also under development.

D. State regulations for control of radiation are more consistent and compatible.

All of the 50 States have radiation control programs whose activities are mandated by State legislation. Nearly all of these have specific regulations for radiation protection activities. It is important that these regulations be sufficiently uniform to enable the States to conduct adequate protection programs and that State regulations be compatible with various Federal requirements. In conjunction with the Conference of Radiation Control Program Directors, an organization comprised of the representatives from State and local radiation control agencies, the FDA's Bureau of Radiological Health coordinates the development of Suggested State Regulations for Control of Radiation. Over 40 States have developed comprehensive radiation control regulations based on the use of this model; these regulations address x-ray equipment manufactured both before and after the promulgation of the Federal performance standard.

REGARDING JUDGMENT IN ORDERING EXAMINATIONS...

A. Medical students and practicing physicians are receiving better training in good radiation practices.

Part of the unnecessary radiation exposure received by patients derives from the sometimes insufficient training received by physicians regarding the judgment to be used in selecting patients for radiologic examinations, conducting radiologic procedures, and interpreting the final results. To help improve this situation, FDA (under a contract with the University of California) has developed a comprehensive learning system to teach all the elements of x-ray usage, including radiation protection, to medical students and practicing physicians. This system, called the Radiological Health Sciences Learning Laboratory (RHSLL), serves as an effective "pipeline" for disseminating the Agency's radiation protection messages to physicans in training.

Thus far, 49 medical schools (approximately half of those in the United States) have purchased the learning laboratory, and an additional 26 orders are on hand. Several foreign countries have also purchased the system. It is anticipated that by 1980 a learning laboratory will be in every U.S. medical school. Approximately 7,000 medical students and radiology residents presently use the learning laboratory each year.

B. More is known about the quantitative risks of certain x-ray procedures.

The Agency's action programs are based upon the underlying assumption that radiation exposure, even at low levels, can pose some biological risk. Quantifying these risks, especially from x-ray procedures that deliver relatively high radiation doses, is important in establishing FDA priorities and providing a firm scientific basis for its actions.

Mammography, a relatively high-dose examination, is presently employed to examine the breasts of approximately 2 million American women annually for the purpose of early cancer detection. Considerable concern has arisen about the possibility of inducing breast cancer as a result of this x-ray exposure. Thus, it is vital to have a quantitative estimate of the risk in order to formulate a rational approach to the use of this diagnostic technique. In this connection, FDA has studied recent data on breast cancer in women following radiation exposure and developed a risk/benefit analysis of mammographic screening for breast cancer that sheds some light on the potential risk of screening asymptomatic women in the general population. The data reveal that there may be no measurable benefit of screening asymptomatic women under 50 years of age, yet upwards of 15 cancers/100,000 women could appear as a result of the radiation dose from such screening. One of the resulting public health actions has been the conclusion by public health authorities that asymptomatic women under 50 years of age not receive routine screening, since they would accrue more damage from the resulting radiation exposure than could be offset by the benefit of early detection of tumors.

C. Women and their physicans are becoming more aware of the problems associated with x-ray exposure during pregnancy.

Although it has been known for many years that the developing embryo or fetus is especially sensitive to radiation injury, physicians often order abdominal x-ray examinations for women without realizing that they are (or may be) pregnant. Good practice dictates that the physician should ascertain the pregnancy status of a young woman when an abdominal radiologic examination is being considered. Nonetheless, several studies have shown that the physician frequently fails to find out about pregnancy before ordering radiologic procedures that might place the unborn child in the direct x-ray beam.

The FDA is developing an approach toward reducing the amount of unintentional abdominal irradiation of pregnant women that emphasizes the collective responsibilities of the referring physician, the patient, the radiologist and the x-ray technologist. For the referring physician and radiologist, the Agency is developing recommendations for the clinical management of pregnant and potentially pregnant patients. For the patient, we are developing educational programs stressing the need to inform the doctor of a possible pregnancy. And for the x-ray technologist, we are developing educational packages to improve practices that keep exposure to a minimum. Should the recommendations result in a one-third reduction in the number of x-ray procedures conducted during pregnancy, approximately 100 cases of childhood cancer would be averted each year. Assuming an average cost of $10,000 in medical costs per cancer case, this would result in a saving of 1 million dollars per year.

REGARDING TECHNIQUES IN PERFORMING EXAMINATIONS...

A. Dental patients are receiving less unnecessary radiation exposure during x-ray examination because of improved quality control.

Because of poor x-ray techniques, including inadequate development of films, a substantial proportion of the population has been receiving unnecessarily high radiation exposure from dental x-ray examinations. To deal with this problem, FDA has developed the Dental Exposure Normalization Technique (DENT) program, a dose reduction project which is carried out by State and local radiation control agencies. A simple radiation measuring device is mailed to all of the dental offices in the State or local jurisdiction, and is exposed by the dentist as though he were radiographing a patient. The device is mailed back to the radiation control agency, where it is evaluated. Dental facilities with abnormally high exposures are then visited by an agency representative and corrective actions are suggested. Presently, the DENT program is being used to monitor about 75,000 dental x-ray machines constituting approximately two-thirds of those in the United States. States which have completed the DENT program have reported an average reduction in patient exposure of approximately 40 percent.

B. Women receiving mammography will be assured of receiving minimum radiation to the breast.

Mammography (x rays of the breast) are presently being performed on large numbers of women for the early detection and diagnosis of breast cancer. Investigations have shown a wide variation in radiation exposure of the breast from these examinations from facility to facility, with unnecessarily high exposures often being delivered because of poor x-ray techniques. To help correct this, the FDA has developed a monitoring program called Breast Exposure: Nationwide Trends (BENT), designed to be carried out by State and local radiation control agencies in a manner similar to the DENT program described above. In this project, radiation measurement devices are mailed to hospitals and offices where mammography is conducted, and are exposed to x rays that a woman would receive during mammography. When the devices are returned to the radiation control agency and the radiation exposure determined, those facilities with unusually high or low exposures are visited for corrective action. This program has demonstrated that it can significantly reduce the radiation dose to the breast from mammography, sometimes as much as tenfold. The program is now being tested in 5 States and 15 more are ready to begin with support from the National Cancer Institute. It is hoped to expand the program so that all 50 States will participate over the next 2 years. It is estimated that a nationwide program will avert 40 deaths from radiation-induced cancer each year, saving at least $400,000 in direct health care costs.

C. Better quality assurance procedures in medical facilities will result in less radiation exposure and better x-ray diagnoses.

A recent evaluation of the Government's black lung (pneumoconiosis) program indicated that as many as 50 percent of the x-ray films of miners submitted by nonradiologist physicians in connection with this project were of such poor quality as to be diagnostically unusable. Bureau surveys have shown that x-ray films of poor diagnostic quality are often accompanied by unnecessarily high patient exposure. The sources of poor film quality are varied and complex, and the Agency has initiated a program to determine common reasons for inadequate radiographs and to develop simple, effective methods that practitioners and x-ray technologists can use to assure quality work. Through the FEDERAL REGISTER mechanism, the FDA will formally recommend that facilities institute qualtiy assurance programs. As the tools and techniques for quality assurance procedures are developed, they will be made available to those who need them. Assuming that 7-8 percent of the approximately 500 million medical x-ray films produced annually are repeated because of poor quality assurance, eliminating these unnecessary retakes will lead to yearly savings of at least 144 million dollars.

D. X-ray technologists are receiving improved training in protecting their patients.

Various surveys have shown that x-ray technologists commonly employ poor radiation protection practices, leading to unnecessary radiation exposure of persons undergoing x-ray examinations. Practices such as failure to use gonad shielding, failure to restrict the size of the x-ray beam to the size of the anatomical part being examined, and the use of a wide range of exposures for the same type of examination all contribute to this unnecessary exposure. These poor practices are due in large measure to inadequate training or inadequate motivation regarding radiation protection. To upgrade the technologist's knowledge and concern in this area, FDA has developed a standard syllabus on radiation protection to be used in all x-ray technologist schools. FDA has also designed and produced a series of packaged training kits on radiation protection and made them available through the National Audiovisual Center to both schools of radiologic technology and hospitals. To deal with the problem of those technologists already in practice, a voluntary system for the continuing education of x-ray machine operators is being developed.

Approximately 1,500 of the packaged training kits have been sold and it is estimated that 10,000 to 12,000 individuals view this material each year. When the system for continuing education is completed, it will reach about 20,000 of the estimated 75,000 credentialed x-ray machine operators annually.

E. The general population will be receiving less exposure of the reproductive organs because of better utilization of gonad shielding.

During 1970, approximately 5 million abdominal x-ray examinations were received by boys and men under the age of 45 in the United States. In approximately 27 percent of those procedures a substantial x-ray dose was received by the testes because of their location in or adjacent to the x-ray field. Much of this exposure, which increases the risk of genetic damage, is unnecessary, and could be avoided through the use of gonad shielding. Yet the limited data available on the use of gonad shielding show that it is employed in less than one-third of the x-ray examinations where it would be appropriate.

To encourage increased use of gonad shielding, FDA has developed guidelines on the use of shielding and published them in the FEDERAL REGISTER as a medical recommendation. This information was recently provided to all U.S. radiologists. In addition, the Agency is working with professional organizations to promote the use of shielding. Implementation programs have also been instituted in Federal medical facilities. Assuming a 50 percent utilization rate for gonad shielding, the present value of future health care costs averted is at least $900,000.

F. A safer form of radioactive iodine is now available for diagnostic use.

The radioisotope iodine-131 traditionally has been employed for many years to study the thyroid gland in patients. Iodine-123, another radioactive form of iodine, can yield the same diagnostic results with only a small fraction of the radiation dose to the patient. However, this type of iodine is difficult to produce in large enough quantities for widespread use. With the assistance of

NASA, FDA developed a new production method for iodine-123 that can produce usable quantities of a highly pure form of this material. Due in part to this effort, iodine-123 is now commercially available for thyroid studies. Through publications and professional conferences, the FDA is encouraging clinicians to use iodine-123 in place of iodine-131. If one-third of the 300,000 radioiodine procedures are performed with iodine-123, it can be estimated that health care savings from averted thyroid cancers will be approximately 1 million dollars each year.

G. Patients receiving radiation therapy will be assured of accurate dosage.

Radiation therapy is used primarily to treat various forms of cancer. It is estimated that approximately 300,000 persons are treated annually with radioactive sealed sources such as cobalt-60. In order to successfully treat the tumor and spare normal adjacent tissue from needless irradiation, therapy machines must be accurately calibrated in advance, and the dose delivered to the tumor site carefully calculated. A variation in radiation dose of as little as 8-10 percent may result in failure to cure, or in an unnecessarily high incidence of side effects. It has been estimated that 30,000 people per year who should be cured are not because of errors such as inaccurate dose delivery.

The FDA has conducted two surveys of radiation therapy equipment which have disclosed that while most facilities can deliver an adequately precise dose, unnecessary errors in dose calculation and in dose delivery do occur in some instances. For example, 5 percent of the units surveyed could not deliver a dose within plus or minus 10 percent. This can be extrapolated to estimate that 10,000 treatments annually are potentially ineffective. As a result of these investigations, the Agency has published in the FEDERAL REGISTER a "Notice of Intent" to develop regulations or recommendations for therapy equipment used in the treatment of cancer.

VI. WHAT ARE THE RESULTS OF FDA'S EFFORTS WITH CONSUMER PRODUCTS?

A. Viewers of color television need no longer be concerned about x-ray exposure.

X rays may be produced when electrons are accelerated by high voltage in a vacuum. Since many of the components in television sets operate at thousands of volts, there is potential for x-ray generation and the escape of these x rays from the receiver cabinet or picture tube. This is the source of the radiation that today makes TV sets a potential even though relatively small hazard.

Approximately 13 million TV sets were manufactured for the U.S. market in 1976. It is estimated that there is an average of more than one television set in every home in the United States. Virtually the entire U.S. population could be exposed to x radiation from poorly designed TV sets. Using assumptions about viewing time, viewing population, viewing distance and an estimation of viewer exposure, it can be calculated that 16 cancer deaths per year could have occurred as a result of unnecessary radiation leakage from television receivers in the absence of the FDA standard.

In May 1967, the Public Health Service announced that 110,000 color TV sets of a particular manufacturer had the potential for emitting x radiation at levels in excess of the industry's own voluntary standard. The Bureau of Radiological Health subsequently found that 6 percent of the color TV sets it tested in the Washington, D.C. metropolitan area emitted x radiation in excess of the industry standard. These findings contributed to the introduction and eventual passage of P.L. 90-602, the Radiation Control for Health and Safety Act of 1968.

A performance standard for television receivers was published on December 25, 1969, and became effective on January 15, 1970. It applies to all television receivers, not just to color TV, and limits the amount of x radiation that can be emitted from the external surface of the set when it is operated under the most extreme conditions.

The millions of TV sets now manufactured each year for the United States emit virtually no x radiation under normal household use. The FDA's enforcement efforts have controlled TV x radiation by assuring that the industry will use conservative TV component and circuit designs. The effectiveness of the standard has been demonstrated through a review of manufacturer reports, inspections of TV manufacturing plants, and in-house laboratory tests. When the Agency occasionally finds TV receivers that fail to comply with the standard, the manufacturer must initiate corrective actions to bring the product into compliance. Twenty-five defect or noncompliance actions have been taken since 1969. These actions involved more than 480,000 TV receivers which had the potential to emit x rays in excess of the allowable limits prescribed by the standard. Thus, these TV receivers no longer pose a health hazard.

B. Owners of microwave ovens can no longer be exposed to hazardous levels of radiation.

The manufacture of microwave ovens has increased from an estimated 40,000 in 1968 to more than 1½ million units in 1976. Today, millions of people use microwave ovens in their homes, in institutions, and in commercial establishments. It is estimated that more than 11 million ovens will be in use by 1980.

Users of certain early models of microwave ovens may have been exposed to unnecessary radiation from leakage around the oven door or from failure of the oven to turn off when the door was opened. Surveys performed in 1969 showed that a significant percentage of microwave ovens leaked in excess of the voluntary industry standard. Microwave radiation of the type produced by microwave ovens can produce biological damage, including cataracts. These survey results led to the promulgation of a performance standard for microwave ovens that became effective in 1971.

The standard has resulted in overall improvements in oven design. For example, door seals, safety interlocks, door latches, and door hinges are now greatly superior to those on pre-1971 ovens.

The FDA monitors compliance with the standard by reviewing manufacturer reports, inspecting manufacturing plants, and testing ovens at the manufacturing site and in FDA laboratories. Microwave ovens are also tested on a sampling basis in actual use in homes.

Since the effective date of the standard, over 60,000 ovens have been found in noncompliance and have been corrected.

C. **Airline personnel and passengers are not being exposed to x rays from baggage inspection systems.**

The use of x-ray systems for security surveillance purposes evolved from the introduction of x-ray equipment in airports for screening hand carried luggage. Since the first units were installed in early 1973, the numbers have grown to an estimated 477 units in routine service at one-third of major U.S. airports. Approximately two hundred million passengers board airplanes annually in the United States. Coupled with the anticipated increased usage of similar x-ray devices in other public facilities, a majority of the United States population may come into contact with these devices.

These systems are located in areas accessible to the general public. Operators have had little or no training in radiation safety, and heavy reliance must be placed on engineered safeguards, rather than administrative controls. Radiation safety problems could arise from external leakage of radiation, access to the primary x-ray beam, or safety system failure.

The FDA began its investigation of the safety of these devices shortly after their introduction into U.S. airports in early 1973. In many systems, it was found that leakage and scatter radiation to both operator and passenger was excessive, and that the means provided to prohibit entry of personnel into the primary x-ray beam was inadequate or nonexistent. Without FDA controls, it would be possible for operators to accumulate an exposure of about 30 R. In 1974, the Agency published a performance standard applicable to baggage x-ray systems, with an effective date 15 days following publication. There have been no reports of accidental exposure as a result of system failure, and field survey data indicate that radiation levels fall below that required by the standard. Therefore, virtually no radiation hazard exists for either operators or airline passengers.

D. Laser devices are being better designed for safety.

A growing variety of commercial laser products are used for the demonstration of physical and optical properties in scientific education; the transfer of intense levels of energy to materials; cutting and drilling; and reading, storing, transmitting, and displaying information in communications.

In view of the knowledge of the serious eye and skin injuries associated with accidental exposure to laser radiation, FDA developed a performance standard for laser products that became effective in August 1976. The standard requires the elimination or containment of laser radiation that need not be accessible for the performance of the intended function of the laser product. For laser radiation that must be accessible, the standard requires an indication of the presence of laser radiation, certain means to control radiation, and adequate warnings to all personnel of the potential hazard, through the use of product labels and instructions.

Assurance of compliance with the standard is made possible through a unique transportable measurement system developed by the Agency. Compliance actions thus far have resulted in product corrections and recalls, including a laser telecommmunications facsimile device used by one of the major news wire services.

E. People will not risk eye damage from mercury vapor lamps.

Mercury vapor lamps are used widely for lighting in public places, including gymnasiums, sports arenas, streets, shopping centers, and industrial facilities. Should the outer glass envelope of the lamp be broken, it may continue to operate and can emit intense short wavelength ultraviolet radiation. Exposure to this radiation can cause skin and eye burns. Over 200 individuals have reportedly sustained injuries from faulty mercury vapor lamps.

Upon receiving reports from State officials of injuries from broken mercury vapor lamps in school gymnasiums, FDA provided interim safety recommendations to State agencies for further dissemination to concerned State officials, particularly in the schools. Performance standards are being developed that will require the lamps to be designed so that the inner ultraviolet-emitting tube cannot operate once the outer glass envelope is broken or damaged. Manufacturers of lamps which do not incorporate such a safety feature will, under the standard, be required to warn consumers through the use of advertisements and product labels that these types of lamps should be installed in settings where people cannot be exposed.

F. The risk of injury from sunlamps will be reduced.

An estimated 800,000 to 1 million sunlamps are sold each year in the United States. These devices emit ultraviolet radiation which is necessary for skin tanning. Overexposure to ultraviolet rays causes immediate deleterious effects such as skin and eye burns, and has been associated with an increased incidence of skin cancer. Individuals with certain medical conditions and those undergoing treatment with certain photosensitizing drugs are particularly susceptible to this type of radiation.

Based upon reports from manufacturers and available biological evidence, a performance standard for this electronic product has been proposed to insure its safe use. The proposed standard requires the use of a timer and protective eyewear, limits the amount of unnecessary short wavelength ultraviolet radiation, and provides users with adequate safety instructions.

VII. WHAT CONCERNS US ABOUT THE FUTURE?

Over the past few years, the technology associated with radiation-producing devices and applications has undergone rapid change, potentially exposing more and more individuals to an ever wider variety of radiation sources. Unfortunately, our knowledge of the hazards of these newer devices and applications, or of the ways they can most safely and effectively be used, is not always complete enough to form the basis for public health action. Thus, the FDA's new program initiatives must be undertaken gradually as the uncertainties in our knowledge are filled. These can best be considered in three categories: (1) uncertainty regarding the indications for medical radiation procedures; (2) the effects of new technology; and (3) uncertainty regarding the biological consequences of exposure.

A. Uncertainty regarding the indications for medical radiation procedures.

The FDA's activities in reducing unnecessary medical radiation exposure have thus far largely centered around improving equipment and techniques. However, it is becoming increasingly apparent that a significant amount of needless exposure (and needless health care costs) can be attributed to the ordering of unnecessary radiologic examinations. Part of this problem is due to forces beyond our immediate control, such as medico-legal (malpractice) pressures that may cause physicians to order additional diagnostic studies. But a major reason for prescribing unnecessary radiologic examinations may be that physicians do not have at their disposal adequate scientific criteria for judging when and when not a particular x-ray or nuclear medicine procedure may be useful.

Although the FDA has made some initial progress in this area by developing ordering criteria for specific population screening procedures (e.g., mass chest x-ray screening), little has been done with respect to radiologic examinations as they are used to diagnose an illness in a specific individual. In fact, a successful methodology to develop these criteria has yet to be developed. This is an important area that calls for attention in the future, should resources permit.

B. The effects of new technology.

The Agency's primary responsibility with respect to changes in technology is to assure that new devices and applications are designed, manufactured, and used in as safe a manner as possible. This sometimes requires us to develop new radiation measurement techniques and tools, to revise existing equipment performance standards or to develop new ones, and to selectively promote those new technologies that can contribute to lowered population exposure.

An example of a technological development that can inherently help to reduce radiation exposure is the advent of a new type of intensifying screen. Intensifying screens contain a substance that emits visible light when exposed to x rays. When a screen is placed next to an x-ray film, the visible light emitted by the screen helps to darken the film. This permits the operator to use a lower x-ray exposure to produce an adequate image on the film, and at the same time reduces the exposure of the patient. The great majority of x-ray examinations are presently conducted using these screens. In recent years, a new class of intensifying screens using rare-earth phosphors has become commercially available which has the potential to reduce patient exposure by about one-half of that produced by today's conventional screens. It is easy to see that the magnitude of the possible exposure reduction on a national basis would be very large, if successful integration of this new technology into clinical practice were achieved. To accelerate this process, the FDA has demonstrated the exposure reduction potential of rare-earth screens, and is promoting their use among the medical community through professional conferences and publications.

One of the more dramatic examples of new technology has been the recent introduction of computed tomography (CT) scanning, in which an x-ray device and a minicomputer are combined to produce an improved image of internal body structures. The number of these devices is expected to increase sharply in the future (see Section III). FDA has identified and must deal with several radiation exposure problems associated with CT scanning. Among these are amendments to the Federal Performance Standard for x-ray machines; adequate techniques for surveying and evaluating CT equipment; appropriate quality assurance procedures which CT users should employ; education of physicians and technologists; and the issue of the efficacy of CT examinations versus conventional x-ray procedures.

C. Concerns about the biological consequences of exposure.

Although an impressive body of knowledge has accumulated documenting the biological effects of various types of radiation, there are still areas in which hazards are suspected but risks are not quantifiable. When this situation applies to a widely used medical procedure that exposes large numbers of people, there is an obvious need to acquire further biological information without delay in order to assure safety to the public. Diagnostic ultrasound is a case in point. Harmful effects in humans have not as yet been demonstrated from the levels of ultrasound used in medical diagnostic tests. But available data is sufficient to raise at least some concern about the safety of ultrasound diagnosis, although present information is insufficient to conclusively define the degree of risk, if any. It is essential that the Agency continue to move forward in evaluating the possible hazards from diagnostic ultrasound, particularly since this modality is widely used in obstetrics; it has been estimated that over 250,000 unborn children are exposed to diagnostic ultrasound in the United States annually.

As scientific information becomes available that sheds new light on the biological risks of radiation exposure, the FDA's priorities and action programs must be adjusted accordingly, with greater emphasis placed on certain equipment and uses, and perhaps less attention devoted to others. One area of present research investigation is the possible association between diagnostic procedures using radioactive iodine-131 in children and subsequent cancer of the thyroid gland. This national study is being carried out by FDA along with the Nuclear Regulatory Commission, the National Cancer Institute, and the Environmental Protection Agency. Should the investigation disclose a cause-effect relationship, the Bureau will take appropriate action.

A similar case, in which preliminary evidence suggests a possible hazard, is the use of photodynamic inactivation to treat infections with the herpes simplex virus. This treatment requires applications of a photosensitizing dye to the viral lesions, followed by exposure of the treated lesions to visible light. Some preliminary work in the FDA's research laboratories suggests a possible long-term risk of cancer from this treatment. This early information has been provided to the medical community via the FDA Drug Bulletin, and further laboratory research to confirm the existence of a hazard is underway.

Even visible light may not be without potential hazard. Recent research has indicated that visual function may be acutely sensitive to damage from fluorescent lamps containing a large component of blue light. Indeed, the entire area of health effects from various sources of visible light on visual function is unknown.

Concern has recently been expressed concerning the possible hazards of electronic products in the radiofrequency range, including short-wave diathermy and various currently uncontrolled broadcast antennas. No definitive information in this area is presently available, and research is required. The FDA is presently asking a group of outside experts to provide advice on whether existing information on the biological effects of microwave radiation can be applied to the radio-frequency range. A negative response would leave this question with little hope of resolution in the immediate future.

Finally, an intriguing possibility suggested by some current research is that there may be substantial numbers of persons who possess a hypersensitivity to long-term radiation injury, but who are at present indistinguishable from the general population at large.

VIII. WHERE TO FROM HERE?

To sum up, we have two responsibilities, now and in the future. The first is to continue to assure compliance with present regulatory standards and to promote widespread adoption of existing voluntary recommendations. The second is to keep abreast of evolving technology and its associated biological risks, and to shape our programs accordingly. In this way, consumers can continue to be assured that their exposure to radiation is at the lowest achievable level commensurate with the expected benefits. Stated in another way, it is the responsibility of FDA's Bureau of Radiological Health to make certain that the advantages conferred upon our society by its technology are not compromised by products or uses that result in unnecessary or unproductive radiation.

Dr. **Kennedy.** At the outset, it is useful to distinguish between regulation and recommendation. We use regulations to assure product safety. These are authorized under Public Law 90-602 and that authority has been since broadened somewhat by the Medical Device Amendments of 1976 to the Food, Drug and Cosmetic Act, which have extended that authority to include total X-ray systems; for example, X-ray film processors.

In the medical area, we have a diagnostic X-ray standard and are now considering the same for radiation therapy and for ultrasound.

In the nonmedical area we have standards for television sets, for cold-cathode tubes, microwave ovens, X-ray baggage inspection systems, cabinet X-ray machines, and lasers.

Recommendations, by contrast, are used to improve user practices in the areas where regulations of user behavior by the traditional tools used by regulatory agencies are inappropriate either because they are beyond the existing tradition for Federal authority or because we are walking into areas in which the development of new techniques and exercise of judgment on the part of practitioners is an important part of the enterprise and one with which governments is traditionally loath to tamper.

Recommendations are being developed, for example, for gonad shielding, for the use of X-rays in pregnancy, for the radiation treatment of benign diseases, for mammography screening, for mass chest X-rays, for the qualifications of X-ray technologists, for exposure guides for X-ray procedures.

I would now like to describe a few of our previous programs, taking those that I outlined at the beginning, in turn and starting, Mr. Chairman, with our biological research program.

The object of this program, in brief, is to study and to estimate the human risk from low-level radiations. We use the results both to set priorities on programs and to justify regulatory actions.

I am going to be very brief in my treatment of these matters, Mr. Chairman, because I know that the subcommittee has heard testimony from Dr. Stewart and from others of the investigators who have made the main advances in these areas.

Dr. Stewart's work and others, of which the committee has heard in previous testimony on this subject, have been projects funded in part by the Food and Drug Administration. As you know, pre-natal exposure to developing experimental rodents produces visible defects in the range of 5 to 12 rads, and studies on humans of the kind I mentioned have shown delayed effects in the range of a half a rad to two rads.

FDA is running its own program on the best sensitive animal model available, the beagle dog, by cooperative study with Colorado State University; a very long-term study that is now half completed and which is described in further detail in our testimony. We are already observing excess cancers, including malignant lymphomas in irradiated animals in this study. When it is completed, it should provide us with the most sensitive index we have to sensitivity in this animal model. We hope it will provide an experimental underpinning for human data, suggestions for epidemiological work, and so on.

FDA has also supported studies on the incidence of thyroid cancer following radiation treatment for ringworm. This permitted some epidemiological studies to be done and demonstrated a fivefold risk increase for thyroid cancer associated with exposures in the range of 6 to 9 rads. This increased our concern about possible effects of certain diagnostic procedures and resulted in our developing a recommendation using a different radioactive isotope of iodine for such diagnostic procedures because of its lower emission energy.

In the area of mammography exposure, we supported studies of radiation-induced breast cancers from fluoroscopy used in the treatment. We developed a mathematical model for risk estimation and for risk benefit calculations for mammography. You and your colleagues know, I am sure, that this model was used by the National Cancer Institute in developing screening guidelines, which are now well known, and suggested restriction of the procedure to women over 50, and have resulted in the United Nations' indications for symptomatic younger women.

I will submit for the record, Mr. Chairman, a report on FDA's bioeffects research in this area, if I may.

Mr. ROGERS. Yes, without objection.

[Testimony resumes on p. 263.]

[The following information was received for the record:]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20857

A SUMMARY OF EXPERIMENTAL AND EPIDEMIOLOGICAL RESEARCH ON IONIZING RADIATION BIOLOGICAL EFFECTS

* * * * * * * * * * * * *

Prepared for:

Subcommittee on Health and the Environment
Committee on Interstate and Foreign Commerce
U.S. House of Representatives

May 1978

INDEX OF CONTENTS

A. Epidemiologic Studies

Project Description

(a) Analysis of the Oxford Survey of Childhood Cancers

(b) Childhood Cancer in Relation to Prenatal Irradiation

(c) National Natality and National Fetal Mortality Survey - U.S. 1979

(d) Breast Cancer and Other Malignancies Following Multiple Fluoroscopies

(e) Risk/Benefit Analyses of Mammography and Other Radiation Procedures

(f) A Follow-Up Study of Persons Who Had Iodine-131 and Other Diagnostic Procedures During Childhood

(g) Controlled Follow-Up Study of Persons Treated for Thyrotoxicosis with Therapeutic Iodine-131 or Surgery

(h) Delayed Effects of Scalp X Irradiation Thyroid Tumor Risk from Scalp X Irradiation

(i) Follow-Up Study of Irradiated Tinea Capitis Cases

(j) The Cooperative Thyrotoxicosis Therapy Follow-Up Study

(k) Radiation Registry of Physicians

(l) Current Trends in Survivorship of Radiologists

(m) Mortality from Cancer and Other Causes Among Men Who Served as X-Ray Technologists in the U.S. Army During World War II

(n) Effects of Intrauterine Radiation on Mortality and Leukemia in Children

(o) Relationship Between Incidence of Leukemia and Exposure to Diagnostic Radiation

(p) Neoplasms in Irradiated Human Populations

(q) Social Security Disability Study

(r) Second Generation Effects from X Rays of Human Female Fetuses

(s) Late Effects of Retention of Thorium Dioxide in Humans

(t) The Effects of Fallout Radiation on the Thyroid Glands of Nevada, Utah, and Arizona School Children

B. Experimental Studies

Project Description

(a) Study of Long-Term Effects in the Beagle Dog From Whole Body Exposure to Ionizing Radiation-Collaborative Radiological Health Laboratory

(b) Effects of In-Utero Exposure

(c) Promotion of RNA Virus Leukemia by Ionizing Radiation

(d) Automated Cytogenetic Radiation Health Monitoring

(e) Erythroid Effects of Radiation in the 10R Range

(f) Studies of Dose-Effect Relationships for Chromosomal Aberrations in Peripheral Blood Lymphocytes After Total and Partial Body Gamma Irradiation

(g) Behavioral Effects of Ionizing Radiation

(h) RBE of Monoenergetic Neutrons

(i) Dose Response in Thyroid Tumor Induction from Iodine-131 and Localized Thyroid and Pituitary Irradiation in Rats

June 1, 1978

BUREAU OF RADIOLOGICAL HEALTH
EPIDEMIOLOGIC STUDIES ON LONG TERM EFFECTS OF LOW LEVEL IONIZING RADIATION

PROJECT	PURPOSE/OBJECTIVE	PRINCIPAL INVESTIGATOR	DURATION (YEARS)	SUPPORT	FINDINGS
MEDICAL, DIAGNOSTIC					
Analysis of the Oxford Survey of Childhood Cancers	To study etiology of cancer deaths among children under 15 in Great Britain.	Alice M. Stewart, M.D. University of Birmingham, England (Contract and Intramural) (NCI)	1972 to present	$350,839	Prenatal exposure to low radiation doses (0.5-2 rad) is associated with a 40-50% increase in risk of childhood leukemia & possibly the same level of increased risk for all childhood cancers. Findings from this study are a basis for present recommendations for the use of radiation in pregnancy.
Effects of Intrauterine Radiation on Mortality and Leukemia in Children	To determine the mortality experience in children exposed to diagnostic x-rays in utero.	E. Diamond, Ph.D. The Johns Hopkins University (Research Grant)	1959-1968	$523,720	The death rate from leukemia was about three times higher for the exposed white children than for the white controls.
Second Generation Effects From X-rays of Human Female Fetuses	To ascertain whether x-ray exposure during fetal life affected the subsequent development of human females and their female offspring.	Mary B. Meyer, Dr.P.H. The Johns Hopkins University (Research Grant) (NICHD)	1972-1978	$207,523	A preliminary statistically significant increase in fertility has been observed in the exposed women.
Risk/Benefit Analyses of Mammography	To study the lifetime risk/benefit balance of the use of mammography in screening for breast cancer.	Richard P. Chiacchierini, Ph.D. Bureau of Radiological Health (Intramural)	1976 to present	$ 30,000	The benefits in person-years of life from screening with both mammography & physical examination exceed the radiation risk for asymptomatic women aged 50 years and over. A dose reduction from 5 to 1 rad per examination leads to an estimated 10% increase in the net benefit for women over 50 years of age if they are screened annually.

PROJECT	PURPOSE/OBJECTIVE	PRINCIPAL INVESTIGATOR	DURATION (YEARS)	SUPPORT	FINDINGS
MEDICAL THERAPEUTIC					
The Cooperative Thyrotoxicosis Therapy Follow-up Study (TT Study)	To determine if persons treated for hyperthyroidism with Iodine-131 are at increased risk of developing malignant neoplasms compared with unexposed patients.	The Cooperative Thyrotoxicosis Study Steering Committee (Contract and Intramural)	1961-1969	6 million	The study population totaled 36,170 patients treated for hyperthyroidism from 1946 through 1964. After an average follow-up period of 7-8 years, those treated with radioactive iodine did not show an increase in leukemia from a low bone marrow dose of 7-15 rads, compared with patients treated by other means. The study ceased data collection in 1968. Further follow-up and analysis is underway at one of the participant institutions.
Neoplasms in Irradiated Human Populations	To assess the risk of neoplasms in persons treated for benign conditions.	Louis H. Hempelmann, M.D. University of Rochester (Research Grant) (NCI)	1965-1979	$814,033	1) This study provided the first indication of thyroid cancer induction by relatively low levels of x-radiation, 20 rads, in infants irradiated for enlarged thymus. 2) The incidence of cancer of the breast following x-ray treatment for acute post-partum mastitis was also increased. Results have been used in developing risk/benefit ratios for mammography.
Breast Cancer and Other Malignancies Following Multiple Fluoroscopies	To determine whether there is a relationship between the radiation dose received during fluoroscopies and risk of developing breast cancer.	George B. Hutchison, M.D. Harvard University (Contract and Intramural) (NIEHS)	1975-1976	$127,363	Breast Cancer was induced by radiation from repeated fluoroscopic examinations during treatment by artificial pneumothorax for tuberculosis. Results have been used in developing risk/benefit ratios for evaluation of mammography as a screening test for breast cancer.

PROJECT	PURPOSE/OBJECTIVE	PRINCIPAL INVESTIGATOR	DURATION (YEARS)	SUPPORT	FINDINGS
Follow-up Study of Irradiated Tinea Capitis Cases	To assess the long-term health experience of 2,404 children with tinea capitis (ringworm of the scalp) who were treated by x-ray of the scalp compared with 1,794 cases not so treated.	Roy E. Albert, M.D. New York University (Research Grant)	1964-1972	$526,349	Benign and malignant tumors and psychiatric disorders were in excess in the irradiated group. The principal low level effect was an excess, although not statistically significant of leukemia associated with a bone marrow dose of 30 rads.
Thyroid Tumor Risk from Scalp X Irradiation During Childhood	1) To determine whether scalp x irradiation in children has long term carcinogenic and behavioral effects. 2) To study the relationship between low dose x irradiation of the thyroid and the risk of thyroid neoplasia.	Baruch Modan, M.D. Sheba Medical Center (P.L. 480 Research Contract and Intramural)	1968-1977	$323,873	To date, published results have covered the late carcinogenic effects. The most noteworthy low-dose effect is the more than 4-fold increase in thyroid cancer associated with a thyroid dose of 6-9 rads. The risk was significantly greater for children exposed under the age of 6 years than for older children.

BEST COPY AVAILABLE

PROJECT	PURPOSE/OBJECTIVE	PRINCIPAL INVESTIGATOR	DURATION (YEARS)	SUPPORT	FINDINGS
OCCUPATIONAL					
Mortality from Cancer and Other Causes Among Men Who Served as X-Ray Technologists in the U.S. Army During World War II	To assess the long term effects of occupational exposure to x-rays in military x-ray technologists.	Seymour Jablon National Academy of Sciences (Contract) (NCI)	1974-1978	$56,680	The study shows that [illegible] of lung cancer mortality [illegible] probably not increased within the limits of the period of observation but raises the possibility that the latent period for this cancer may have been shortened by occupational exposure to x-rays.
Radiation Registry of Physicians	To investigate the long term effects of chronic exposure to low levels of ionizing radiation among radiologists.	Gordon Jessup, Ph.D. Bureau of Radiological Health (Contract and Intramural) (AEC/NCI)	1968-1976	$309,813	All living members as of 1961 of medical specialty societies in radiology and pathology have been queried about their exposure and health status, and the health of their family members. Data analysis is in progress
Current Trends in Survivorship of Radiologists	To determine if radiologists have an increased risk of death from non-specific aging and from specific causes of death.	Gevevieve M. Matanoski, M.D., Dr. P.H. The Johns Hopkins University (Research Grant) (NCI)	1971-1973	$53,356	Compared to other medical specialists, there is an excess in mortality rates for all causes for radiologists who entered the specialist societies before 1940 but not for later entries. An excess in cancer mortality among radiologists persists in all cohorts from 1920 through 1949. Except for lymphoma, no other specific site of cancer is consistently higher.
Mortality of New England Dentists (1921-1960)	To determine the mortality of dentists in comparison with that of the general population and of physicians.	Robert L. Glass, D.D.S. (Contract)	1965-1966	not available	No life-shortening or excess radiation-associated malignancies was found

PROJECT	PURPOSE/OBJECTIVE	PRINCIPAL INVESTIGATOR	DURATION (YEARS)	SUPPORT	FINDINGS
NUCLEAR FALLOUT					
The Effects of Fallout Radiation on the Thyroid Glands of School Children in Southwestern U.S.	To determine if radiation exposure from fallout radioiodines as a result of nuclear weapons testing in Nevada in the 1950's was associated with an increased risk of thyroid neoplasms in exposed children. Children in southwestern Utah and Nevada (exposed) and in Arizona (relatively unexposed) were studied.	Marvin Rallison, M.D. Utah State Department of Health (Research Grant)	1965-1970	$109,456	This study was completed in 1972. No increased risk was found for thyroid neoplasms associated with fallout exposure and an estimated average thyroid dose of 17 rads. However, the period of follow-up was short and the sample size of exposed and unexposed children small.
BACKGROUND RADIATION					
Background Radiation in the Etiology of Congenital Malformations	Study of births and infant deaths in 3 states (Col., Michigan & Minnesota)	L.M. Schuman, M.D. University of Minnesota (Contract)	1961-1967	not available	No correlation between background radiation and congenital malformations could be established.

LONG TERM EPIDEMIOLOGICAL STUDIES RECENTLY INITIATED OR TO START

PROJECT	PURPOSE/OBJECTIVE	PRINCIPAL INVESTIGATOR	DURATION (YEARS)	SUPPORT	FINDINGS
A Follow-Up Study of Persons Who Had Iodine-131 and Other Diagnostic Procedures During Childhood	To assess the possible delayed adverse effects of exposure to diagnostic levels of Iodine-131.	B.S.H. Harris, III Research Triangle Institute (Contract and Intramural) (NRC - Present) (NCI - Present) (EPA - Earlier)	1976-1981	$1,875,000	This multi-institutional study is in the early stages of data collection. The results should provide a basis for evaluating established medical practice and national environmental emission standards.
National Natality and National Fetal Mortality Survey, U.S. 1979	To ascertain the frequency of exposure during pregnancy to ionizing & nonionizing radiation including ultrasound; to study the associations between these radiation procedures and possible adverse effects such as congenital anomalies or low birth weight in live births and fetal deaths.	Paul L. Roney Bureau of Radiological Health (Interagency Agreement) (NICHD) (NIOSH)	1977-1981	$470,000	A pretest of the study is planned in the fourth quarter of 1978 with the study starting January 1, 1979. Data will be available in 1981. The study population is a sample of U.S. live births and fetal deaths.
Childhood Cancer in Relation to Prenatal Irradiation	To assess the possible relationship between prenatal irradiation and the occurrence of cancers in children similar to the Oxford Survey of Childhood Cancers (OSCC), but without possible bias caused by socioeconomic status and maternal recall of her x-ray experience.	Seymour Jablon National Academy of Sciences (Contract) (NCI)	1975-1978	$ 35,000	Data have been collected and analysis is underway. The study subjects are wives of U.S. servicemen.
Controlled Follow-Up Study of Persons Treated for Thyrotoxicosis With Therapeutic Iodine-131 or Surgery	To determine whether women treated for hyperthyroidism with therapeutic doses of Iodine-131 are at increased risk of developing malignant neoplasms than women treated for the same condition by surgery and/or anti-thyroid drugs.	Leonard T. Kurland, M.D., Dr. P.H. Mayo Foundation (Contract and Intramural)	1977-1978	$ 62,050	This will add ten years of observation to the Thyrotoxicosis study and may permit an evaluation of the dose-effect characteristics of I-131.

PROJECT	PURPOSE/OBJECTIVE	PRINCIPAL INVESTIGATOR	DURATION (YEARS)	SUPPORT	FINDINGS
Relationship between Incidence of Leukemia and Exposure to Diagnostic Radiation	To detect the possible relationship between exposure to low levels of ionizing radiation and induction of leukemia	Tadeusz Majle, M.D.,Ph.D. National Institute of Hygiene Warsaw, Poland (P.L. 480 Research Contract)	1974-1980	$276,000	A pilot study has demonstrated the feasibility of conducting the full scale study, of estimating organ doses from standard x-ray procedures, of administering a questionnaire by trained interviewers and of recovering records showing the diagnostic x-ray procedures which were performed. Full scale study is now underway.
Further Analysis of Case-control Study of Adult Leukemia and Other Cancers in Relation to Diagnostic Radiation	To assess the possible relationship between exposure to low levels of ionizing radiation and leukemia induction	Alice M. Stewart, M.D. University of Birmingham Birmingham, England (Contract)	1977-1978	$ 25,000	An earlier analysis reported an association between some forms of adult leukemia and exposure to diagnostic procedures using ionizing radiation.

EPIDEMIOLOGIC STUDIES

TITLE: Analysis of the Oxford Survey of Childhood Cancers

INVESTIGATOR: Alice M. Stewart, M.D.

INSTITUTION: University of Birmingham, Birmingham, England

CUMULATIVE DOLLAR SUPPORT: $350,839 (includes in-house costs)

DURATION: 6/55 - Present

OBJECTIVE: To analyze cancer deaths among children under 15 in Great Britain.

APPROACH: Each year the Survey obtains death information from the General Registrar's office for all children who died under 15 years of age from cancer. A control child who survived is selected based on year of birth, geographic area of birth and sex. Questionnaires are sent to the district medical officers who interview the mothers, and additional information is collected from prenatal clinics and hospitals.

RESULTS: Positive association between cancer mortality among children and diagnostic levels of prenatal irradiation (about 1 rad increases risk of mortality by 40-50%).

Extensive analyses have been made to rule out extraneous factors such as social class, the reasons for the maternal x-rays, and birthweight. Better estimates of the true risk by considering the time of the x ray (e.g. preconception, duration of pregnancy) will result from analyses currently underway. Children who died of leukemia were found to have had, on the average, more episodes of infective diseases than children who died of solid tumors or the surviving controls.

IMPACT: Findings from this study are a basis for present recommendations for women to advise their physicians if they are or may be pregnant where medical x rays are being considered. Physicians are advised to consider whether, in the event that a patient is or may be pregnant, a proposed x ray should be postponed or an alternative diagnostic procedure should be used.

TITLE: Childhood Cancer in Relation to Prenatal Irradiation

INVESTIGATOR: Seymour Jablon

INSTITUTION: Medical Follow-Up Agency of the National Research Council/National Academy of Sciences

CUMULATIVE DOLLAR SUPPORT: $35,000 (includes in-house costs)

DURATION: 10/73 - 6/76

OBJECTIVE: To assess the possible relationship between prenatal irradiation and the occurrence of cancers in children similar to the Oxford Survey of Childhood Cancers (OSCC), but without possible bias caused by socioeconomic status and maternal recall of her x-ray experience.

APPROACH: Initial funding was from the Bureau of Radiological Health; subsequent major funding was from the National Cancer Institute. Births in military hospitals were used to minimize socioeconomic differentials and abstracts of hospital charts were used to minimize the effect of maternal recall. From an NCI file of 39,000 cancer deaths among children under 15 years of age, about 1,000 deaths in military hospitals were identified. Two random controls were selected for each cancer death, matched to the death on hospital and year of birth. From the medical records, information on x rays, maternal age, mode of delivery, drugs and other possible relevant characteristics have been abstracted.

RESULTS: Data have been collected and analysis is underway.

IMPACT: When results become available, they will be used in the on going reviews of the medical practice of taking x rays during pregnancy. If necessary, Bureau recommendations will be revised.

TITLE: National Natality and National Fetal Mortality Survey U.S. 1979

INVESTIGATOR: Paul L. Roney

INSTITUTION: Bureau of Radiological Health, Rockville, MD

CUMULATIVE DOLLAR SUPPORT: $470,000 (includes in-house costs)

DURATION: 7/77 - 1981

OBJECTIVE: To ascertain the frequency of exposure during pregnancy to ionizing and nonionizing radiation including ultrasound; to study the associations between these radiation procedures and possible adverse effects such as congenital anomalies or low birth weight in live births and fetal deaths.

APPROACH: This is an interagency project involving collaboration between NICHD, NIOSH, FDA, and NCHS. In cooperation with the National Center for Health Statistics, a 1 in 500 sample of the live births, and 1 in 4 sample of fetal deaths of 28 weeks or more of gestation in 1979 in the United States will be queried. Questionnaires covering of demographic and medical care questions will be sent to the attending physician, the institution of birth, the mother and all other physicians and dentists identified as providing health care during pregnancy. The BRH portion of the project relates to use of radiation during the year preceding delivery and comparison of radiation experience in live births and fetal deaths.

PROGRESS: Five questionnaires have been developed and coding procedures are being prepared. An interagency agreement with the National Center for Health Statistics is being negotiated.

PLANS: A pretest of the study is planned in the fourth quarter of 1978 with the study starting January 1, 1979. Data will be available in 1981.

IMPACT: This study will document the use of x rays during pregnancy, an important period of human development. Through comparison with earlier surveys, this study will show whether the use of x rays during pregnancy is increasing, decreasing or remaining the same. By using the combined questionnaires from the different medical sources, the indications for the radiological procedure and the mode of delivery including pregnancy complications will be examined. The differences in radiation experience between live births and fetal deaths will be documented. These findings along with others will form a basis for recommendations on the use of several forms of medical radiation during pregnancy.

TITLE: Breast Cancer and Other Malignancies Following Multiple Fluoroscopies

INVESTIGATOR: George B. Hutchison, M.D.

INSTITUTION: Harvard School of Public Health, Boston, MA

CUMULATIVE DOLLAR SUPPORT: $127,363 (includes in-house costs)

DURATION: 5/75 - 8/76

OBJECTIVE: To determine whether there is a relationship between the radiation dose received during fluoroscopies and risk of developing breast cancer; to determine whether susceptibility to late radiation effects is related to age at exposure.

APPROACH: The study entailed a followup of 1,764 female patients who were discharged alive from two tuberculosis sanatoria in Massachusetts between 1930 and 1954. The study population included 1,047 women who had been exposed to an average of 102 fluoroscopic examinations of the chest in the course of pneumontherapy and a control group of 717 women who were treated by other procedures, such as surgery or drugs. A 1975 mailing address or death certificate was obtained for 93.6 percent of the subjects. Questionnaires sent to the 1,146 living patients resulted in a response rate of 78 percent. Estimates of radiation dose to the breasts of exposed patients involved measurements on old fluoroscopic units, personal interviews with physicians who performed the examinations, and application of an absorbed dose calculation scheme.

RESULTS: This study has shown an association between women who had repeated fluoroscopic examinations during treatment by artificial pneumothorax for tuberculosis and subsequent breast cancer. The study is being continued under the auspices of the National Cancer Institute. They have also been used to alert patients and physicians to the fact that these patients are at greater risk of breast cancer and should be examined periodically.

IMPACT: The results of the study affected the risk/benefit estimates used in evaluating breast cancer screening using mammography.

TITLE: Risk/Benefit Analyses of Mammography and Other Radiation Procedures

INVESTIGATOR: Richard P. Chiacchierini, Ph.D.

INSTITUTION: Bureau of Radiological Health, Rockville, MD

CUMULATIVE DOLLAR SUPPORT: $30,000 (all in-house costs)

DURATION: 7/76 - Present

OBJECTIVE: To study the lifetime risk/benefit balance of the use of mammography in screening for breast cancer.

APPROACH: A mathematical model of a life table has been developed and computerized to analyze the problem. The model utilizes generalized estimates which can be adjusted to reflect different levels of effectiveness.

PROGRESS: The current model has resulted in two risk/benefit analyses which have been published and a third which is being readied for publication. The benefits from screening with both mammography and physical examination exceed the radiation risk for asymptomatic women aged 50 years and over and the benefit is enhanced if the dose can be reduced without damaging the quality of the x-ray film. A dose reduction from 5 rads to 1 rad per examination leads to an estimated 10% increase in the net benefit for women over 50 years of age if they are screened annually. The National Cancer Institute's Consensus Panel on Breast Cancer Screening used estimates from this work, in their recommendations on screening to the NCI Breast Cancer Detection Demonstration Projects. In addition, the most recent analysis has identified hypothetical benefit estimates for each age and radiation dose group for which the radiation risks would be equalled or exceeded. Such results are useful in the design of future clinical trials of mammography screening.

IMPACT: This work formed part of the data base from which the NCI guidelines on mammography screening to the BCDDP's were issued. It provides a quantitative justification for the mammography dose reduction activities implemented by the Bureau of Radiological Health and supports the national guidelines on mammography screening being developed by BRH.

Risk/benefit analyses based on work like that described here will contiue to affect health care policies of Federal agencies in their recommendations to the medical community and the public.

TITLE: A Follow-Up Study of Persons Who Had Iodine-131 and Other Diagnostic Procedures During Childhood

INVESTIGATOR: B.S.H. Harris, III

INSTITUTION: Research Triangle Institute, Research Triangle Park, NC

CUMULATIVE DOLLAR SUPPORT: $1,875,000 (reflects $1M through IAG with Nuclear Regulatory Commission, $.5M through IAG with National Cancer Institute, and $375,000 in-house costs)

DURATION: 9/76 - 9/81

OBJECTIVE: To assess the possible delayed adverse effects of exposure to diagnostic levels of Iodine-131.

APPROACH: This is a cooperative effort with funding provided by the Nuclear Regulatory Commission and the National Cancer Institute. The project is a collaborative multi-center study of children who were exposed to Iodine-131 for diagnostic purposes between January 1, 1946, and December 31, 1967, and two control groups. The controls are: (1) children of similar age, race, sex, and disease state not exposed to diagnostic I-131; and (2) siblings of the exposed children. The project is an extension and expansion of one conducted under the auspices of the Environmental Protection Agency (EPA). Upon identification of the study groups, the project will locate, followup, and query the health status of the subjects. Medical and demographic information is being abstracted from hospital records, and death certificates will be obtained for patients who died.

From EPA, data have been obtained for about 1,000 persons exposed to I-131 for diagnostic purposes prior to 1961. Eighteen medical centers have been contacted by the Bureau of Radiological Health and have agreed to cooperate in the expanded project. Development of patients rosters and abstracting of medical records is underway. Data collection activities will continue. Analysis and preparation of reports will be carried out by the Bureau of Radiological Health.

RESULTS: Study is in the early stages of data collection. There are no available results.

IMPACT: The results of this study will provide a basis for evaluating established medical practice and national environmental emission standards.

TITLE: Controlled Follow-Up Study of Persons Treated For Thyrotoxicosis With Therapeutic Iodine-131 or Surgery

INVESTIGATOR: Leonard T. Kurland, M.D., Dr.P.H.

INSTITUTION: Mayo Foundation, Rochester, MN 55901

CUMULATIVE DOLLAR SUPPORT: $62,050 (includes in-house costs)

DURATION: 7/77 - 7/78

OBJECTIVE: To determine whether women treated for hyperthyroidism with therapeutic doses of Iodine-131 are at increased risk of developing malignant neoplasms than women treated for the same condition by surgery and/or anti-thyroid drugs.

APPROACH: The study population consists of women treated for hyperthyroidism at the Mayo Clinic between January 1, 1946, and December 31, 1964. This is a follow-up study of patients in the following treatment groups: 1,004 treated with Iodine-131; 2,141 treated surgically; 426 who received both Iodine-131 and surgical treatment; and, 125 who received anti-thyroid drugs.

The medical records of these patients are being abstracted. Dosimetric information is being collected for patients treated with Iodine-131 in order to estimate various organ doses. Procedures to validate causes of death have been developed. Follow-up of patients will be by telephone and by mail questionnaire.

Both morbidity and mortality analyses will be conducted. Validation of neoplasms reported on the questionnaire will be attempted by obtaining confirmatory information from medical records and pathological reports and specimens, when available.

IMPACT: If an association is found between exposure to Iodine-131 and cancer in organs with low doses, then the radiation risks from low-level Iodine-131 will be re-evaluated. Results from this study will permit an evaluation of the dose-effect characteristics of I-131.

TITLE: Delayed Effects of Scalp X Irradiation Thyroid Tumor Risk From Scalp X Irradiation

INVESTIGATOR: Baruch Moden, M.D.

INSTITUTION: Chaim Sheba Medical Center, Tel Hashomes, Israel

CUMULATIVE DOLLAR SUPPORT: $323,873

DURATION: 6/68 - 3/77

OBJECTIVE:

1) To determine whether scalp x irradiation in children has long term carcinogenic and behavioral effects.
2) To study the relationship between low dose x irradiation of the thyroid and the risk of thyroid neoplasia.

APPROACH: This is an epidemiologic followup study of children in Israel who received x-ray treatment for ringworm of the scalp years ago. The study population consists of 10,842 cases who had scalp irradiation for tinea capitis between 1948 and 1960 (1-15 years of age at the time of treatment) and two matched control groups, one selected through the Central Population Registry (10,842) and the other consisting of non-irradiated, non-tinea siblings (5,400). The records of all cases and controls have been checked against hospital, tumor registry, welfare, mental hospital, school, and other records. A sample of cases and controls has received clinical examinations.

RESULTS: To date, published results have covered the late carcinogenic effects. They show a significantly increased risk of both malignant and benign neoplasms of the head and neck region in the irradiated group as compared to the controls. The most striking increase is seen in brain, parotid and thyroid tumors. Because the thyroid dose (6.5 rads) was the lowest ever reported to be carcinogenic, dosimetry was repeated and a more intensive search for thyroid tumors undertaken. The thyroid dose was again found low (4.3 to 9.9 rads), the marked excess of thyroid cancer was confirmed for a 25-year study period (1950-1974), and an age effect was demonstrated showing the risk for neoplasms higher among children x-rayed below the age of six years.

IMPACT: At average thyroid doses of only 6 to 9 rads, there was more than a 5-fold increase in thyroid cancer in irradiated children compared to controls. Furthermore, the risk was significantly greater for children exposed under the age of six years than for older children. The demonstration of thyroid cancer induction from low-level x radiation must influence radiation protection practices for medical and other exposures.

TITLE: Follow-Up Study of Irradiated Tinea Capitis Cases

INVESTIGATOR: Roy E. Albert, M.D.

INSTITUTION: Institute of Environmental Medicine, New York University Medical Center, New York, NY

CUMULATIVE DOLLAR SUPPORT: $526,349

DURATION: 12/64 - 11/72

OBJECTIVE: To assess the long-term health experience of 2,404 patients with tinea capitis (ringworm of the scalp) who were treated by x ray of the scalp compared with 1,794 cases not so treated. The purpose is to characterize the nature and magnitude of chronic radiation injury due to x-ray epilation (removal of hair).

APPROACH: The exposed and control groups were treated between 1940-1958 at the New York University Hospital Skin and Cancer Clinic.

The study includes:

a) An evaluation of the medical experience of the irradiated and control populations by means of a health questionnaire;

b) a clinical and laboratory examination of a representative sample of the irradiated and control population; and

c) a study of the x-ray dose to the various head structures associated with the x-ray treatment for tinea capitis.

RESULTS: Eighty percent of the study group (exposed and controls) has been located, at an average of 15 years after treatment. Fourteen cases of cancer, five of whom died, have occurred so far in the exposed group compared with one case (still living) in the controls. Cancers in the irradiated group included 4 leukemias, 3 brain tumors, and 2 carcinomas of the scalp. Psychiatric disorders were confirmed in 3.2% of the irradiated group compared with 1.27% in controls. The major differences between the two groups were personality disorders and psychoneuroses. No evidence of increased damage to eyes or ears was observed in the exposed group.

The average scalp dose was 800 rads. The dose to the brain ranged from 150 rads at the surface to 50 rads at the base. Doses to the eyes, ears, and cranial marrow were 50, 70, and 435 rads, respectively.

IMPACT: The data establish a firm relationship between radiation exposure and subsequent cancers. The results suggest that mental illness may be a manifestation of residual brain damage from ionizing radiation. X-ray treatment for tinea capitis is no longer practiced.

TITLE: The Cooperative Thyrotoxicosis Therapy Followup Study (TT Study)

INVESTIGATOR: The Cooperative Thyrotoxicosis Study Steering Committee

INSTITUTION: Twenty-six clinical centers in U.S. and Great Britain

CUMULATIVE DOLLAR SUPPORT: $6,000,000 (includes in-house costs)

DURATION: 6/61 - 12/69

OBJECTIVE: To determine if persons treated for hyperthyroidism with I-131 are at increased risk of developing malignant neoplasms compared with unexposed patients.

APPROACH: Data were collected at 26 medical institutions in the United States and England on patients treated for hyperthyroidism between January 1, 1946, and December 31, 1964. For each patient an abstract was prepared, of the detailed course of hyperthroidism, its treatment, a history of all radiation exposure, and other diseases. Patients were recalled for physical examinations. A death certificate was obtained for each patient that died.

RESULTS: The study ceased data collection in 1968. The study population totaled 36,170 patients treated for hyperthyroidism from 1946 through 1964. Information on the current health status or a death certificate was obtained for 96.5 percent of this population. The distribution of patients by treatment group was 54% treated with I-131; 32% by surgery; 10% by a combination of surgery and I-131; and 4% by drugs only. The average length of followup in the I-131 group was 6.5 years and 10.6 years in the surgical group. The age- and sex-adjusted rate of leukemia was 13 per 100,000 person-years in the surgical group. Based on these data, there was no significant difference between the two groups. There was also no significant difference between the two groups in the rate of thyroid cancer.

IMPACT: The study was conducted for a period too short to yield definitive answers; several unresolved issues remain.

TITLE: Radiation Registry of Physicians

INVESTIGATOR: Gordon Jessup, Ph.D.

INSTITUTION: Bureau of Radiological Health, Rockville, MD

CUMULATIVE DOLLAR SUPPORT: $309,813 ($10,000 awarded to National Academy of Sciences, $23,400 awarded to American College or Radiology, $53,395 to College of American Pathologists, $223,000 for in-house costs)

DURATION: 10/68 - Present

OBJECTIVE: To investigate the long term somatic (bodily) and genetic effects in humans of chronic exposure to low levels of ionizing radiation.

APPROACH: Radiologists who are occupationally exposed to ionizing radiation and a non-exposed comparison group, pathologists, have been queried by mail. Two questionnaires have been completed by the same physicians, with a minimum interval of five years. Information collected includes demographic characteristics; occupational, personal, and family radiation exposure; somatic effects of radiation such as injuries; leukemia and other cancers; and genetic effects such as numbers and sex of children, pregnancy wastage, and congenital defects. Project review is provided by a National Academy of Sciences - National Research Council Advisory Committee which is supported by FDA contract.

RESULTS: A descriptive overview of the first questionnaire was published in 1971, and although it furnished several suggestive leads the data at that time were not adequate to draw firm conclusions. The data from the second questionnaire have been compiled, and several papers are being developed. The first of these show that radiologists and their families have a higher frequency of personal medical diagnostic and therapeutic radiological procedures than do pathologists and their families. This is one area where non-occupational use of ionizing radiation can be reduced.

IMPACT: This type of information is useful in evaluating the effectiveness of current safety standards and in indicating possible modifications. Results from this project will also provide information that may be helpful in quantifying the low dose region of the dose-response curve for ionizing radiation.

TITLE: Current Trends In Survivorship of Radiologists

INVESTIGATOR: Genevieve M. Matanowski, M.D., Dr.P.H.

INSTITUTION: The School of Hygiene and Public Health, Johns Hopkins University, Baltimore, MD 21205

CUMULATIVE DOLLAR SUPPORT: $53,356

DURATION: 7/71 - 6/73

OBJECTIVE: To determine if radiologists have an increased risk of death from non-specific aging; to compare the risk for radiologists who entered the specialty after newer safety methods were introduced to those who were in practice earlier; and to ascertain if any specific causes of death were increased.

APPROACH: In 1965, Drs. Seltser and Sartwell reported that the death rates of radiologists were higher than those of other physician specialists for the time period 1935-1958. The same relationship existed for cancer, cardiovascular-renal disease and all other causes. The present study extended the period of observation through 1969. Data were secured from death certificates and causes of death reported to the Americal Medical Association.

RESULTS: The data were analyzed by 10-year cohorts with individuals grouped according to year of entry into the specialist societies. Persons in the 1950-59 and 1960-69 cohorts have not been in the study long enough to assess possible effects of low level radiation.

The following results relate to the cohorts from 1920 through 1949:

1. Compared to other specialists, there is an excess in mortality rates for all causes for radiologists who entered the specialist societies in 1920-29 and 1930-1939 but not for later entries.

2. An excess in cancer mortality among radiologists in comparison with other specialists was found to persist in all cohorts from 1920 through 1949. Leukemia mortality rates were higher among radiologists in the 1920-29 and 1930-39 cohorts, but not in the later cohort. Mortality from lymphoma was higher among radiologists in the 1930-39 and 1940-49 cohorts, but not in the earlier cohort. Mortality from no other specific site of cancer was consistently higher in two or more cohorts.

IMPACT: This study documented an occupational hazard for radiologists. Through papers in professional journals, the radiologic profession was informed of the increased risk associated with their past experience. The effectiveness of of current safety standards cannot be judged until more time has passed for the 1950-59 cohort.

TITLE: Mortality from Cancer and Other Causes Among Men Who Served as X-Ray Technologists In the U.S. Army During World War II

INVESTIGATOR: Seymour Jablon

INSTITUTION: National Academy of Sciences, Washington, D.C.

CUMULATIVE DOLLAR SUPPORT: $56,680 (includes in-house costs)

DURATION: 6/74 - Present

OBJECTIVE: To assess the long term effects of occupational exposure to x rays in military x-ray technologists compared to a similar age group of military medical laboratory and pharmacy technologists.

APPROACH: An earlier study by the Medical Followup Agency (National Academy of Sciences, National Research Council) was made of an exposed group (6,500 x-ray technologists) and a control group (6,826 medical laboratory and pharmacy technologists). The period of observation ended with the year 1963. The present project extends the period of observation through 1973 to further explore possible delayed adverse effects. The project analyzes death rates by cause of death, based on information obtained from the Veterans Administration. The data have been collected and a report has been submitted to the Bureau of Radiological Health by the Medical Followup Agency. Further analysis is proceeding within the Bureau of Radiological Health.

RESULTS: The earlier study indicated a need to study the possibility that mortality from lung cancer may be increased as a result of occupational exposure to x rays. The later study shows that the risk of lung cancer mortality is probably not increased within the limits of the period of observation but raises the possibility that the latent period for this cancer may have been shortened by occupational exposure to x rays.

IMPACT: The results of this study of chronic low level radiation will be used to formulate the Bureau's position on radiation protection of occupational groups exposed to x irradiation. Such standards will be developed jointly with the National Institute of Occupational Safety and Health (NIOSH) of CDC.

TITLE: Effects of Intrauterine Radiation on Mortality and Leukemia in Children

INVESTIGATOR: A.M. Lilienfeld, M.D.

INSTITUTION: Johns Hopkins University, Baltimore, MD

CUMULATIVE DOLLAR SUPPORT: $523,720 (includes in-house costs)

DURATION: 11/59 - 6/68

OBJECTIVE: To determine the mortality experience in children exposed to diagnostic x rays in utero.

APPROACH: About 20,000 children who were exposed to intrauterine x rays from 1947 to 1959 were traced to determine their mortality experience. In comparison about 35,000 children not exposed and matched by selected characteristics were traced in a similar manner.

RESULTS: The death rate from leukemia was about three times higher for the exposed white children than for the white controls. In contrast the mortality experience of the black exposed children was not greater than their controls.

IMPACT: Information derived from this study has been incorporated into proposed Bureau recommendations to physicians advising them to consider the possible pregnancy status of their women patients when they feel that abdominal x rays are needed. In addition, public relations statements via posters and radio-spot announcements have been directed to women instructing them to inform their physicians if they might be pregnant. The physician decides whether the condition of the patient requires immediate x rays, whether the x rays can be delayed or whether other methods of diagnosis can be substituted.

TITLE: Relationship Between Incidence of Leukemia and Exposure to Diagnostic Radiation

INVESTIGATOR: Tadeusz Majle, M.D., Ph.D.

INSTITUTION: National Institute of Hygiene, Warsaw 36, Poland

CUMULATIVE DOLLAR SUPPORT: $150,000

DURATION: 10/76 - 9/80

OBJECTIVE: To study leukemia in adults with regard to previous exposure to radiation used for medical and dental diagnosis.

APPROACH: The study will pay particular attention to dosimetry of the diagnostic equipment and procedures used. One thousand cases will be drawn from the files of the cancer registry at the Institute of Oncology and an equal number of controls will be drawn from population census files. The controls will be matched to the cases on age, sex, and occupation and if deceased, the year of death. Subjects or a close relative of deceased subjects will be interviewed and a questionnaire will be completed by a trained interviewer. A pilot study has been completed in which the methods have been tested. The full scale study is now being initiated.

IMPACT: If the occurrence of leukemia is positively related to observed low-level doses, recommendations for additional radiation controls will be developed.

TITLE: Neoplasms In Irradiated Human Populations

INVESTIGATOR: Louis H. Hempelmann, M.D.

INSTITUTION: University of Rochester, Rochester, NY

CUMULATIVE DOLLAR SUPPORT: $814,033

DURATION: 4/65 - 12/79

OBJECTIVE: To assess the risk of neoplasms in persons treated for benign conditions.

APPROACH: All three of the following groups had a 15-20 year followup by use of a mail questionnaire and diagnoses were obtained from physicians, hospitals and, at times, death certificates.

a) a 20-year followup of 2,872 persons whose thymus was irradiated in infancy and 5,005 sibling controls;

b) a followup of subjects given radiation treatment to the head (971 given x-ray treatment, 417 treated with radium alone) and 2,746 sibling controls; and

c) a followup of 606 women who were treated with x rays to the breast for acute post-partum mastitis, 554 non-irradiated sisters of the exposed, 539 women who had mastitis but were not treated with x rays and 206 sisters of the unirradiated mastitis cases.

RESULTS: The incidence of both benign and malignant thyroid neoplasms was increased. The incidence of cancer of the breast following x-ray treatment for acute post-partum mastitis was also increased. Data for treatment to the head are too incomplete for analysis.

IMPACT: a) The National Cancer Institute has informed the professional community and the general public about irradiation-related thyroid cancer. The goals are to brief physicians on how to examine, diagnose and treat irradiation-related thyroid tumors, and to urge the U.S. population at special risk of developing thyroid cancer to be examined by their physicians. Two publications have been widely distributed. The American Cancer Society is cooperating in the distribution of a pamphlet for the professional groups, a leaflet for the public has been distributed through supermarkets by a variety of organizations, by physicians, and in response to inquiries to the NCI.

b) None, further followup is planned.

c) The relative risk information as developed in this study was part of the rationale used in developing the risk/benefit analysis for mammography screening for breast cancer and the subsequent recommendations.

TITLE: Social Security Disability Study

INVESTIGATORS: Loren Mills, Kay Barrick, and Richard Chiacchierini

INSTITUTION: Division of Biological Effects, Bureau of Radiological Health, Rockville, MD

CUMULATIVE DOLLAR SUPPORT: $135,000 ($35,000 awarded to Social Secruity Administration, $100,000 for in-house costs)

DURATION: 5/73 - Present

OBJECTIVE: To determine if existing pools of data collected for other purposes (e.g., disability claims) could be used to identify occupational groups for epidemiologic studies of the relation of ill-health to exposure to radiation.

APPROACH: Social Security Disability Claims data were collected for the year 1972. The data were coded directly from the claim forms, verified, and entered into the computer. Available information includes age, age of onset of impairment, race, sex, state of residence, medical diagnosis, occupation, number of years in occupation, and years of education.

RESULTS: These data have yielded an estimated 54,000 target cases in which skin disorders, blood disorders, cataracts, or malignant neoplasms were indicated as primary, secondary, or teritiary diagnoses (diseases of interest). Comparison data have also been obtained for approximately 54,000 control cases that do not manifest any of the diagnoses designated as diseases of interest. This preliminary file has undergone a final screening process, for completed case records, to establish the working file for in depth analyses. The final screening resulted in 77,000 completed case records, approximately half Target and half Control cases for study.

Initial tabular data are being developed relating length of time in occupation to the alleged age of onset of the disease. This has been done for a series of selected diseases and for occupations requiring the individual to work with or in the near vicinity of electronic products that emit radiation. Similar tabular data are also being developed for occupations that have no such identifiable radiation history.

IMPACT: If the data are found suitable, this and other similar studies will provide the radiation protection community with a mechanism to identify occupations associated with excess specific diseases and radiation. The data will lead to more definitive studies and may affect permissable occupational radiation exposure limits.

TITLE: Second Generation Effects From X Rays of Human Female Fetuses

INVESTIGATOR: Mary B. Meyer, Dr. P.H.

INSTITUTION: Johns Hopkins University, Baltimore, MD

CUMULATIVE DOLLAR SUPPORT: $207,523

DURATION: 7/72 - 6/78

OBJECTIVE: To ascertain whether x-ray exposure during fetal life affected the subsequent development of human females and their female offspring.

APPROACH: The study population comprises 1,558 females exposed to x rays in utero and 1,658 unexposed females matched by hospital of birth, parity, race and birthdate (1947-1952). All are black and were born in Baltimore. Live births and fetal deaths are identified by searching the files of the Baltimore City Health Department. In addition, these women are being located and questioned concerning family size, growth, health and disease, reproductive history and use of medical care facilities.

RESULTS: A statistically significant increase (10-15%) in fertility has been observed in the exposed women. Differences remain after adjusting for economic, social and medical factors. A smaller difference in number of pregnancies persisted during the most recent six-year period. The exposed women completed fewer grades of school, had poorer general health, more menstrual problems, more of certain diseases and accidents and are heavier for their height than controls. These are preliminary findings. When data collection is complete the findings will be tested to find whether other factors can explain them.

IMPACT: If the preliminary findings of the associations between exposures to diagnostic x rays in utero and subsequent development and health and in reproductive histories are confirmed through further study, this new information will need to be weighed in the risk/benefit assessment of the use of x rays during pregnancy.

TITLE: Late Effects of Retention of Thorium Dioxide In Humans

INVESTIGATOR: Murray L. Janowen, M.D.

INSTITUTION: Dept. of Radiology, Mass. General Hospital, Boston, Mass.

CUMULATIVE DOLLAR SUPPORT: $96,151

DURATION: 9/67 - 8/70

OBJECTIVE: To establish the morbidity and mortality of 322 patients who received Thorotrast for cerebral arteriography. All living patients are given intensive physical and laboratory examinations to detect delayed sequelae of their radiation.

RESULTS: One hundred and ninety of 195 patients who received Thorotrast at the Massachusetts General Hospital, and 124 of 129 patients who received it at the Lahey Clinic have been identified, located and interviewed. Six malignant tumors have been found in the former population and eight tumors in the latter, none of them of the kind associated with radiation. Forty patients have been examined including physical examination, total body radiography, whole-body counting, chromosome analysis, liver function tests, complete blood count, and morphological analysis, and a variety of other laboratory tests. Frequent abnormalities have been found in alkaline phosphatase, Bromsulphaline retention test, protein electrophoresis, and chromosome analysis. Thorotrast retained in the body is directly related to the amount ingested.

IMPACT: Human data on the effects of chronic low-dose internal emitters are very limited. Most information until this time has been provided by a study of radium dial painters. The Thorotrast population is a unique opportunity to study a large group of patients who carry reasonably well known body burdens. Such information is vital for the establishment of exposure standards in industry and for the general public possibly subject to environmental contaminations.

TITLE: The Effects of Fallout Radiation on the Thyroid Glands of Nevada, Utah, and Arizona Schoolchildren

INVESTIGATOR: Marvin Rallison, M.D.

INSTITUTION: Utah State Department of Health, Salt Lake City, UT

CUMULATIVE DOLLAR SUPPORT: $109,456 (does not include in-house costs)

DURATION: 6/65 - 12/70

OBJECTIVE: To determine if radiation exposure from fallout as a result of nuclear weapons testing in Nevada in the 1950's was associated with an increased risk of thyroid neoplasms in exposed children. Children in southwestern Utah, and Nevada exposed to fallout radioiodines and a relatively unexposed comparison group in central Arizona were identified and studied.

APPROACH: A total of 4,827 schoolchildren in Utah, Nevada, and Arizona were examined by teams of Public Health Service physicians from 1965 through 1968 to determine any evidence of thyroid disease. Those children who on initial screening were abnormal were referred to a panel of three thyroidologists for further evaluation. Questionnaires were completed on each child in the study to obtain relevant medical and demographic data. Cumulative thyroid doses from ^{131}I exposure were calculated for each child to determine if there was a dose-response relationship for the development of thyroid neoplasms.

RESULTS: This study was completed in 1972. No increased risk was found for thyroid neoplasms associated with fallout exposure. However, the period of followup may have been insufficient to document such an association, and the sample size of exposed and unexposed children may have been too small to detect an increased risk.

IMPACT: This is the only large-scale study of children exposed to cumulative radioactive fallout and no association was shown between this exposure and the risk of thyroid neoplasia.

EXPERIMENTAL STUDIES

TITLE: Study of Long-Term Effects In the Beagle Dog From Whole Body Exposure to Ionizing Radiation - Collaborative Radiological Health Laboratory

INVESTIGATOR: Dr. Stephen A. Benjamin

INSTITUTION: Colorado State University, Fort Collins, CO

CUMULATIVE DOLLAR SUPPORT: $14,480,844 (does not include in-house costs)

DURATION: 5/62 - Present

OBJECTIVE: The Collaborative Radiological Health Laboratory (CRHL) was established in 1962 by the U.S. Public Health Service and Colorado State University for the purpose of determining in a carefully contolled animal experiment, the lifetime hazards associated with prenatal and early postnatal exposure to ionizing radiation.

APPROACH: As a part of a long-term study to evaluate the biological hazards associated with low levels of ionizing radiation, beagle dogs were given whole-body exposure to ^{60}Co-gamma radiation at one of 6 ages of pre- or postnatal life.. Four hundred and eighty dogs, 120 for each age at exposure, received 20 R at 8, 28, or 55 days postcoitus (dpc) or at 2 days postpartum (dpp). Similarly 480 dogs, 120 at each age, were exposed to 100 R. Exposures of 100 R were also given to 118 dogs at 70 dpp and 231 dogs at 365 dpp. An additional 360 dogs were sham-irradiated. Both sexes were equally represented. The exposures were given bilaterally, for a total of 10 minutes, and measured as midline in air doses. The absorbed dose was calculated for each dog. Mean values for each age at exposure ranged from 15.6 to 17.5 rads for 20 R exposures and from 80.8 to 88.3 rads for exposure to 100 R.

RESULTS: Mortality due to neoplasia during the initial 10 years of the experiment was examined. Twenty dogs died or were killed because of neoplasia. Five malignant lymphomas, nine carcinomas (three of mammary origin, two of prostatic origin, and one each of oral mucosa, ovary, urinary bladder, and thyroid origin), four sarcomas (two hemangiosarcomas, one fibrosarcoma and one mast cell sarcoma), one astrocytoma, and one hepatocellular adenoma were diagnosed. Neoplasms occurred in all irradiated groups except 8 dpc (20 and 100 R) and 70 dpp (100 R). Eleven neoplasms developed in dogs irradiated perinatally (55 dpc or 2 dpp) with 20 or 100 R.

Four of the tumors in the perinatally irradiated dogs were detected before two years of age. The earliest death was at 3 months, due to an astrocytoma. A single sham-irradiated dog died of a malignant tumor, a mammary carcinoma. Preliminary analyses point to 3 findings of particular interest: (1) the preponderance of malignant neoplasms in irradiated dogs, (2) the unusual finding of four deaths due to neoplasia prior to two years of age in perinatally irradiated dogs, and (3) the occurrence of five malignant lymphomas in this relatively small irradiated population. The statistical analyses of these data are continuing.

IMPACT: The CRHL study occupies a unique position among past and present studies of radiation effects. It is a long-term (life span) study of a moderately large and long-lived mammal exposed at one of several times during development to a relatively small and discrete dose of external radiation. Ages at irradiation for comparison reflect the primary concern with medical exposure during the developmental period. Thus research at this laboratory is primarily concerned with evaluating the role of age as a factor influencing an animal's response to injury. The principal concern is with the long-term effects of a single low-level exposure to gamma radiation during the prenatal or early postnatal life. Its early findings provide experimental support for the results of human epidemiologic investigation which has been a source of controversy.

CUMULATIVE DOLLAR SUPPORT:

	Support through FY 1977	Support for FY 1978	Totals
Colorado State University	$ 2,457,251	$ 264,436	$ 2,721,687
NIH/State Matching Funds	900,016	---	900,016
PHS/FDA/BRH	9,821,041	1,038,100	10,859,141
TOTALS	$13,178,308	$ 1,302,536	$14,480,844

TITLE: Effects of In Utero X-Ray Exposure

INVESTIGATORS: Roberts Rugh, Thomas Withrow, Melvin Stratmeyer, Kenneth Yao, Mary McManaway, Moris Shore, Richard Felten, and Howard Cyr

INSTITUTION: This is an in-house study involving the Metabolic Studies Section and the Genetic Studies Section, Experimental Studies Branch, Division of Biological Effects, Bureau of Radiological Health, Rockville, MD

CUMULATIVE DOLLAR SUPPORT: $95,000 (all in-house costs)

DURATION: 7/72 to Present

OBJECTIVE: Laboratory research and literature reviews have been undertaken to examine several biological effects of in utero x-ray exposure, with particular emphasis on low-dose effects.

APPROACH: The laboratory research involved study of several biological endpoints following the in utero exposure of mice, rats, or Chinese hamsters. A study by Rugh of the sensitivity of the oocyte exposed to x rays prior to conception, then mated to normal males, revealed no significant changes in the number of pups, their body weight, or the number of congenital anomalities. However, some sterility was observed if the matings occurred two months after the exposure. The degree of sterility was related to dose. Another study done by Yao showed that some small decrease in the number of oocytes and the percent of oocytes undergoing meiosis, when these oocytes were irradiated prior to conception. These small changes were not related to the preconception cell stage present at time of exposure. In studies directed by Shore, significant decrease in the survival of pups, their body weight, and their average brain weight were noted following in utero exposure. However, no changes occurred in the amount of total protein in the brain. Studies on the uptake of radioactive labels into the brain and its components gave little information. A major finding has been the production of brain hernias in developing fetuses following exposures earlier in pregnancy of 5, 10, and 25R. The demonstration of a significant anomaly at 5R suggests the extreme sensitivity of the developing fetus.

IMPACT: These studies and many others have been collated and summarized for use as a biological basis document for an Agency recommendation on x-ray exposure during pregnancy.

IMPACT: The research supported by the Bureau continues to support and amplify the concern expressed about the sensitivity of the developing fetus to ionizing radiation. The Bureau has already published notice in the Federal Register notifying the public of its intent to publish a recommendation on irradiation and pregnancy.

TITLE: Promotion of RNA Virus Leukemia by Ionizing Radiation

INVESTIGATOR: Dr. Robert Bases

INSTITUTION: Albert Einstein College of Medicine, Yeshiva Univ, NY

CUMULATIVE DOLLAR SUPPORT: $75,798 (includes in-house costs)

DURATION: 6/74 - 5/75

OBJECTIVE: 1) Determine whether x-ray exposure of mammalian cells, in the presence of infectious RNA tumor virus, enhances cellular integration of virus; 2) determine whether x-ray exposure of mammalian cells induces the release of normally latent RNA tumor virus; and, 3) obtain dose response data for the above endpoints, which can be used in guiding the establishment, or reevaluation of existing performance standards for products emitting ionizing radiation.

APPROACH: Well-characterized in vitro test systems were utilized.

RESULTS:

1. Integration of infectious RNA tumor virus into target cell DNA can be detected.
2. X irradiation of cells prior to RNA tumor virus infection inhibits the entrance of viral RNA into the cell nucleus. However, viral RNA which reaches the cell nucleus can be integrated into cell DNA.
3. The infectious center in vitro assay for detection of virus activation is the most sensitive and quantitative of the assays utilized.
4. X-ray exposure (300-1800 rads) of mammalian cells induces the release of normally latent endogenous RNA tumor virus. The quantity of virus induced was less than that observed with certain chemicals, such as the photosensitizing agent, iododeoxyuridine (IUDR). Thus, radiation induction of latent RNA tumor virus in vitro is an infrequent phenomenon. These findings corroborate the work of other investigators in this field.

IMPACT: One of the currently proposed mechanisms for the initiation of cancer is that an agent such as ionizing radiation causes a normally latent endogenous virus with oncogenic potential to be expressed. The results of this study showed that ionizing radiation does induce latent RNA tumor virus. The work is being continued to investigate other mechanisms of carcinogenesis by ionizing radiation.

TITLE: Automated Cytogenetic Radiation Health Monitoring

INVESTIGATOR: Niel Wald

INSTITUTION: University of Pittsburgh, Pittsburgh, PA

CUMULATIVE DOLLAR SUPPORT: $444,462

DURATION: 3/71 - 4/78

OBJECTIVE: Chromosomes comprise the information system of tissue cells. Radiation induced damage in chromosome structure alters this information by deletion or by code change. This damage can sometimes be microscopically visualized as chromosome aberrations, and it can be expressed as a malfunction of cellular processes. The consequences may range from abnormal cell metabolism to cell death. Chemical and environmental factors can also damage chromosomes, and synergistically potentiate the effects of radiation. Consequently, methods of rapidly assaying chromosomal damage in large numbers of persons are highly desired for public health needs, especially in an agency with broad but interrelated responsibilities such as FDA.

APPROACH: The Bureau of Radiological Health recognized the value to public health activities of a grant application to develop a computer automated system for chromosomal analysis by Dr. Niel Wald, and has been able to support this research since 1971. The system principally consists of an automatic high speed scanning microscope for blood cell preparations, a closed-circuit television system, a control computer, and an analysis computer. A large and significant part of this development has been in the software which directs and interprets the raw data. Generally, cell specimens may be obtained and prepared much faster than they can be analyzed by personnel, and it is in this aspect that the automated methods have their value.

RESULTS: In its present configuration the automatic chromosome analysis system is approximately five times faster than manual scoring techniques, and its accuracy approaches ninety percent. Its principal functions, the location of metaphase cells and the recognition of aberrant chromosomes, is highly dependent on software, and several promising approaches are being investigated to increase intra-system compatibility and accuracy.

IMPACT: Automated screening of chromosome damage has been attempted by several groups for many years. The technical problems are great - for example, to consistently stain the chromosomes has proven to be a great problem. However, such a system would reduce the procedures for screening genetic damage due to ionizing radiation and other environmental stresses. This grant has developed a system that is five times faster than normal procedures and 90% accruate.

TITLE: Erythroid Effects of Radiation In the 10R Range

INVESTIGATOR: Joseph K. Gong

INSTITUTION: State University of New York at Buffalo, NY

CUMULATIVE DOLLAR SUPPORT: FY'76 - $46,301
FY'77 - $41,722

DURATION: 9/76 - 8/79

OBJECTIVE:

1. To determine the lowest dose of an acute x-ray exposure to rats that can consistently elicit an erythroid response. The erythroid response being studied is the quantitative change in the red blood precursor cells of the bone marrow. The erythroid response is being determined both in x-irradiated animals later stressed by removal of 50% of their circulating red cells and those which had not been stressed.

2. To find a subthreshold dose that would invariably result in no change in the bone marrow composition.

3. To determine if a subthreshold x-ray dose given repeatedly until the total dose at least equals that of the determined threshold dose will cause a change in the erythroid response.

RESULTS: In otherwise unstressed animals, a 50 mR acute dose of x rays consistently showed no statistically significant changes (relative to controls) in red blood precursor cells in the bone marrow for a period of 5 to 30 weeks post-irradiation. Doses of 150 mR and higher invariably showed significant changes. In animals under anemic stress (at 5 weeks post-irradiation) the 50 mR dose again showed no significant changes. Doses of 150 mR and higher always showed significant changes. In unstressed animals 150 mR and higher doses showed higher bone marrow levels of red precursor cells and in anemically stressed rats the values were lower than normal.

IMPACT: Dr. Gong has found significant increases in precursor blood cells in normal animals following as little as 150 mR. Such biological change at such low doses is rare, and may indicate a very sensitive system.

TITLE: Studies of Dose-Effect Relationships For Chromosomal Aberrations In Peripheral Blood Lymphocytes After Total and Partial Body Gamma Irradiation

INVESTIGATOR: Julian Liniecki

INSTITUTION: Medical Academy of Lodz, Medical Research Center
Division of Nuclear Medicine and Radio Biology, Poland

CUMULATIVE DOLLAR SUPPORT: $85,992

DURATION: 1/77 - 2/79

OBJECTIVE: Dr. Liniecki has established a method of determining doses delivered to the whole body by culturing blood lymphocytes and examining chromosome aberrations. He is now developing a method for determining biological damage due to partial body irradiation, again using chromosome aberrations as the indicator of damage.

APPROACH: "Phantom" rabbits were constructed, irradiated (whole body or partial body), and dosimetry studies undertaken. Live rabbits were irradiated and chromosome aberrations analyzed as a function of time after exposure and dose. Mixtures of irradiated blood and nonirradiated blood have been analyzed in order to more fully understand the mechanisms behind body exposures.

RESULTS: The relationship between chromosome aberrations and dose has been established for whole body irradiation. Phantoms have been constructed for partial body irradiation. Studies on mixtures of irradiated and nonirradiated blood are now underway, in an effort to derive an understanding of the amount of biological damage (chromosome aberration (dicentrics)) resulting from partial body exposures.

IMPACT: Chromosome aberrations, particularly dicentrics and rings, have been used for sometime as an indicator of total biological damage following radiation exposure. The correlation is fairly good at high doses, but needs more development at low doses and for partial body exposures. Dr. Linecki is having some success in building models which help in the area of partial body exposures. This method is of importance in assessing real biological damage following occupational or therapeutic exposures.

TITLE: Behavioral Effects of Ionizing Radiation

INVESTIGATOR: Ernest Furchtgott

INSTITUTION: University of Tennessee, Knoxville, TN

CUMULATIVE DOLLAR SUPPORT: $153,966

DURATION: 9/57 - 8/71

OBJECTIVE: This research is directed at determining the behavioral effect of ionizing radiation administered during an animal's developmental period.

APPROACH: A variety of behavioral functions, both simple and complex, were investigated during the life time of prenatally exposed rats.

RESULTS: It was found that animals exposed *in utero* were deficient in maze learning, in several types of locomotor tests, in depth and olfactory discrimination, and in adjusting their food or water intake to deprivation schedules. They were hyperactive in novel situations; their heart rate increased more rapidly than that of control animals when presented with novel stimuli; and in general they exhibited behaviors that are usually labeled fearfulness. For locomotor deficits and maze learning, the lowest effective dose was around 25R administered sometime during days 15 to 18 of gestation. The severity of the motor deficits is apparently relatively constant throughout the animal's life-span.

IMPACT: This research shows significant behavioral deficiencies following exposures of 25R during pregnancy. These deficiencies last throughout the lifetime of the rat. The results give us concern that similar mental or behavioral deficiencies could be present in humans at the same dose levels and below. This study again alerts us to the sensitivity of the developing fetus and embryo.

TITLE: RBE of Monoenergetic Neutrons

INVESTIGATOR: Harold H. Rossi

INSTITUTION: Columbia University, New York, NY

CUMULATIVE DOLLAR SUPPORT: $493,693

DURATION: 9/61 - 8/72

OBJECTIVE: The linear, no threshold, dose effect model was originally adopted for radiation protection applications on the assumption that it was conservative. However, radiobiological data were, and remain, both highly varied and incomplete, and no general theory of radiobiology existed beyond the somewhat limited target theory of D.E. Lea. Since radiation protection activities have serious legal and economic impacts as well as value to public health rapid progress in theoretical radiobiology verified by selected physical and biological experiments were needed to test the conservatism of the linear, non-threshold model, especially at low doses.

APPROACH: During the 1950's Dr. H.H. Rossi developed a tissue equivalent proportional counter which yielded data of unusual information content. The analysis of these data led to his development of a theory of microdosimetry which offered new insights in radiobiology. To test the theory and to estimate the usefulness of the linear, no threshold model carefully controlled biological experiments were required to provide first-hand data which would permit an analysis of the dependence of relative biological effectiveness, RBE, on absorbed dose for two quite different kinds of radiations, neutrons and x or gamma rays. To this end the Bureau of Radiological Health, FDA, provided grant support to Dr. Rossi's research.

RESULTS: Experiments on opacification of the mouse lens and selected data from the scientific literature have verified the theory of microdosimetry and led to the development of the theory of dual action. This latter appears to explain much of the radiobiological phenomena, but several outstanding and important areas remain difficult, principally leukemia and mammary neoplasm induction.

IMPACT: The theories of dual action and microdosimetry constitute significant scientific advances necessary to the estimation of absolute and relative risks of ionizing radiation exposure. However, some radiobiological data are thus far not satisfactorily explained, and continued research and caution are advised in the interest of both health and economic aspects of radiation protection activities.

This result shows us some real differences between the mechanisms of interaction of neutrons or alpha particles as compared to x rays. These studies indicate that the biological effects due to neutrons and alphas at low doses may have been underestimated and the biological effects (e.g., cancers) due to x rays at low doses may be presently overestimated. A revision of all risks associated with ionizing radiation has been proposed by NCRP based on these and other similar studies.

TITLE: Dose Response In Thyroid Tumor Induction From Iodine-131 and Localized Thyroid and Pituitary Irradiation In Rats

INVESTIGATORS: W. Lee, R.P. Chiacchierini, N.C. Telles, and B. Shleien

INSTITUTION: Bureau of Radiological Health, FDA

CUMULATIVE DOLLAR SUPPORT: $265,124 (includes in-house costs)

DURATION: 7/76 - 6/79

OBJECTIVE: The Bureau of Radiological Health scientists wanted to examine the risk of thyroid cancer induction from I-131 x-ray irradiations. This study was also designed to investigate whether irradiation of the pituitary gland would influence the radiation response of the thyroid gland, and visa versa.

APPROACH: Three thousand young female rats were used in this study. These animals were irradiated with various radiation doses form either I-131 or x rays to the thyroid, pituitary, or both, and they are to be kept for two years to observe the incidence of thyroid tumor induction from the two types of radiation.

RESULT: These Bureau scientists had developed a new approach to accurately determine thyroid radiation dose from I-131 irradiation. Their dosimetric findings revealed that previous rat thyroid dosimetrics could be in error by 40% or more. Application of their dosimetric findings to other similar studies suggested that the previously reported relative thyroid radiosensitivity of 10:1 for x rays and I-131 radiation may only be 5:1. Animal pathology data will not be available until the end of the study which is scheduled to be completed by March 1979.

IMPACT: Recent epidemiologic findings suggested that thyroid radiosensitivity may be much higher than what we once believed. Currently, patients are routinely exposed from ten to hundreds of rads of I-131 radiation during I-131 thyroid diagnostic procedures. The longterm consequence of this level of thyroid radiation dose is not clear at the present. When the results from this study are incorporated with the findings from the diagnostic and therapeutic I-131 patient followup studies currently in progress within our Epidemiologic Studies Branch, we will be in a strong position to assess the risk from I-131 irradiation.

Dr. **Kennedy**. I will now move to a discussion of the regulatory and advisory activities that we carry out under the terms of Public Law 90-602. As I said before, the regulations that we promulgated under that statute became effective in 1974. The regulation is broad. It covers complete systems as well as 11 separate components. It appliers to 158 factory-based manufacturers who produce about 5,000 models of various components, and it also applies to 2,100 assemblers.

I did not know before I came to this task, Mr. Chairman, that X-ray machines are a little bit like 10-speed bicycles in that many of them are not made by a single manufacturer on a single assembly line, but rather, they are put together from components made by different manufacturers so that you can have some of the better models assembled as systems rather than as single production items. That, in some regards, makes the enforcement task more difficult.

We carry out that task by reviewing reports submitted to us as a regulatory requirement by the industry, by plant inspections, by laboratory testing of instruments and components, and by field testing. I will take these just briefly one by one.

Manufacturers have to give us reports that describe their testing and quality control procedures, the design procedures and the instructions that they give to assemblers and their quality control systems. We review those reports, as the subcommittee has noted in its questions to us, sometimes with a delay, although that is a backlog we are now reducing, I am pleased to say. We identify questionable areas in those reports and use them as one of the bases, but not the only basis, for scheduling plant inspections.

The plant inspections are performed to review manufacturers' testing programs. We have now, under this program visited all domestic and foreign manufacturers of X-ray equipment at least once. We believe we will be able to undertake these visits on an average of at least once every 2½ years.

I might say, parenthetically, the way in which we schedule these depends on our perception of the hazards associated with that particular component. We would not want to make frequent visits to a component manufacturer who made only X-ray tables. On the other hand, for General Electric, we might want to see quite a lot more often than every 2 years.

In the laboratory testing phase of our work, we attempt to measure every aspect of a product's compliance, every item that is small enough to be assembled and brought back home for the work. We will take a dental X-ray whole; we will take components. We would not take an entire X-ray unit out of a hospital, for obvious reasons, for those kinds of tests; we would send a radiological health officer into the field to undertake measurements actually on a unit installed in a hospital or a doctor's office.

Not only are these conducted by FDA staffs in the 10 Federal regions and the constituent districts; they are also done by States under 22 different contracts. And they check the compliance of both factory-based manufacturers and assemblers by looking at the machines where they are.

Ninety-four percent of the machines have been tested within the first year of installation, and we have tested about 15 percent of all certified machines in the field on the ground. There has been a high rate of noncompliance thus far. The overall noncompliance is 30 percent. The noncompliance figure we cite elsewhere for measuring the public health significance is 20 percent, and the difference is due to the fact we are taking a somewhat higher threshold for the measurements that we take for quantitating the serious public health problems. We think that the rate is that high largely because the standard is new and complex and because we think the assemblers and manufacturers are just learning to deal with it.

This program, by the way, is now being expanded with an additional $400,000 in State contracts to increase the proportion of certified machines that are being field tested.

Let me just summarize what our compliance people have found thus far with respect to that performance standard. There have been 72 recalls thus far involving 38,000 products. There have been 26 recalls under the defect provisions of Public Law 90-602, and my testimony gives, on page 15, the details of an example of one such enforcement case, which I won't trouble to go through now.

We think that the standard has required major changes in X-ray machine design and manufacturing practices and that it has, in fact, accelerated technological innovation. One example is automated positive beam limitation, a device which minimizes the extent of X-ray exposure automatically so that the size of the film or the area exposed within the cassette is matched to the size of the beam by reducing the edges of the beam. This eliminates the exposure that the patient might receive that doesn't do any good in terms of creating a record the doctor can use. I think it is fair to say that this has resulted entirely from FDA activities in this performance standard work, and it is becoming standard on machines produced for use in the United States.

I will have more to say later about the kinds of savings that we think are associated with that kind of innovation.

The standard has also, incidentally, forced FDA to develop new test equipment and instruments in-house, including some of the field calibration equipment that we use to test instruments in actual medical installations.

It is an obvious point, but I still think it is worth making, that even the best equipment regulation can't guarantee minimum exposure any more than the most intelligent and conscientiously applied design requirements in the safety features of automobiles can make a car safe in the hands of an unknowledgeable and careless driver.

As a result, we have programs that are designed to improve user practices, both of X-ray prescribers and of equipment operators. And that is a somewhat different problem.

A prescriber may order a procedure that, in terms of a careful cost benefit analysis of that medical situation, is not really a justified procedure. If that could be eliminated, it would represent a saving. An even more obvious saving would be represented if we could, by training operators better, eliminate repeat X-rays or make sure that only the minimum exposure was used that was necessary to generate the adequate diagnostic information for the physician who is using the radiograph. So we think that both these kinds of education are essential.

They consist essentially of voluntary recommendations for good practices and professional and consumer education. Let me give some examples.

In the quality assurance area we essentially address the failure of operators to use good practices. Those programs are largely conducted with the States who are responsible for licensing or certifying such operators where there are State programs.

We also have some particular programs that are designed to improve practice in certain often-performed procedures. I mention just two, which we call by the rhyming acronyms BENT and DENT. DENT stands for Dental Exposure Normalization Technique; and BENT, Breast Exposure: Nationwide Trends. One has the feeling one of these, the second one to go into effect, was invented rather carefully. What they do is try to identify high exposure facilities by looking at those facilities by a rather unique mailing technique.

I have had to resist the temptation to give you a lot of visuals here, Mr. Chairman, because this is an activity that lends itself to small-size demonstrations. I promise not to do too much of this.

But this is a card that can be sent to an X-ray facility. There are instructions for the operator of the facility to expose the button on the card. The button consists of a thermoluminescent dosimeter. It is exposed in the machine and returned on the attached postcard to the Food and Drug Administration, where it is read. The X-ray energy is stored in the crystal. It is released later when the crystal is measured photometrically, and we know if that facility is routinely overexposing patients. And these are usually cooperative programs with the States. The States can be informed or we can help them further with it. We have had good results with those, and the States are enthusiastic about the procedure.

The DENT program has already shown a 40-percent exposure reduction in the States where it has been applied, and we think that BENT is on its way to showing a similar performance improvement.

Recently, Secretary Califano wrote to all Governors of the States either urging continued participation or joining. We have had some more joinings as a consequence of that, and it is now in 44 to 48 States.

A second area where we think there is important room for improvement is in X-ray repeats. National studies have shown that 5 to 10 percent of X-rays are repeated and that many of these are avoidable by quality assurance programs. We pilot-tested one of these at the Baltimore Public Health Service Hospital and have gotten about a 30-percent reduction in retakes in that pilot effort.

As a consequence of that experience, we are developing protocols for processor quality assurance for general use and recommendations which we will issue. We think we ought to be able to get one third of that 10 percent, say, which would be 3 percent of the total exposures controlled, if we can be as successful on a widespread basis as in that pilot program.

Next, I want to talk about the area of professional education. It is fair to say that this is an area in which FDA evolved most slowly, largely because it is one in which Federal involvement has been, for very good reasons, a little hesitant across the board.

There is a special nature to the relationship between physician and patient. One does not want to create in the physicians the view that they are being ordered around by their Government in an area where their training suits them to make judgments.

On the other hand, we have confronted increasing evidence that there is a lot of unnecessary ordering of X-rays, and we have become gradually more and more convinced there is a tremendous amount of room for improvement here. If we can attack the problem successfully, by which I mean in a way that convinces physicians that we are doing something for them that is positive instead of trying to limit their capacity to practice medicine intelligently, we can do a good deal.

A major problem is the lack of scientific efficacy data on when X-rays are useful and when they are not. We have made, in at least one area, a promising start.

You have heard, I think, testimony by Dr. Phillips earlier in this series of hearings. You know that the Seattle pilot project in which definitive criteria were evolved for ordering emergency room skull X-rays for trauma showed a 40-percent reduction initially in those. I believe he testified at these hearings that the results he now believes to be even better than that.

In at least a couple of areas—pelvimetry, of course, routine chest X-rays—there is reason to believe that similar reductions are possible. So eventually, one might be able to go to work on a national overordering figure which is estimated by some students to be 30 percent or so. So there is clearly a lot of opportunity there on which we are only beginning, by educational efforts, to make headway.

I might just say, however, that the areas of continuing medical education and beginning medical education are promising areas to start on this problem. We now have an X-ray technologist radiation protection instruction package that is going to over 10,000 persons a year, and one, for use in medical education, has been purchased and adopted by three-quarters of the medical schools in the United States; and that is not just a casual commitment. We charge—I think $15,000 has to be put down before they get it.

In the area of consumer education, which we think is equally important, it is clear that reduction of exposure is possible by getting patents to be more forthcoming about their situation and more ready to ask questions of a physician or a dentist about the need for having an X-ray.

Everybody agrees, I think, with the need for reducing X-rays in the abdominal region, in view of the possibility that a woman may be pregnant. We have distributed copies of this poster very widely nationally to physicians. many of you who have seen it before will know it is on display in the offices of many obstetricians and gynecologists. The American College of Obstetricians and Gynecologists cooperated fully in this effort with us.

Another consumer effort is an X-ray record card, which we encourage patents to use in order to keep track of their own X-ray examinations and to be able to inform their doctors about previous exams. Multiple ordering is a problem that this kind of device can help with, we think.

It is a delicate task. We want to educate people about the risks and the benefits of X-ray exposure, not frighten them into refusing needed X-ray exams, but encourage them to hold a useful dialog with their physicians, dentists, dental hygienists, whoever, about the need for a particular procedure.

Now, Mr. Chairman, I want to touch briefly on two other subjects in which we know the subcommittee is interested, and then I will summarize and stop.

The first of these has to do with the interagency relationships. We can't help but agree with the subcommittee's assessment that Federal radiation activities could use better coordination. For our own part, we have tried to join with sister agencies to coordinate programs, share resources, and identify problems. We have 29 memorandums of understanding and interagency agreements with other Federal agencies. For example, the National Cancer Institute has worked with us on the BENT program. We have a Memorandum of Understanding with EPA on medical radiation guidance for Federal facilities, under which the Food and Drug Administration will coordinate the Public Health Service implementation of that guidance.

As you may know, Mr. Chairman, this has ended a long period of uncertainty and one might say a dispute between the Department of Health, Education, and Welfare and the Environmental Protection Agency about who has the authority to promulgate such guidance. We essentially said that although we felt there was a great deal of merit, in our view, on the appropriate disposition of the problem, that that was one of those cases in which neither party had so much of a right to be right that it could be allowed to stand in the way of getting the agencies together and getting to work on that.

I think we gave enough to get a program going, although we are still not convinced that the appropriate division was made. We are now working on the problem.

We have close relationships with the States on programs like BENT and DENT and on contract inspection programs. We have produced, along with NRC, with EPA and with Occupational Safety and Health Administration, and the States, model regulations for State programs in a number of cases.

I want to add that in addition to producing some distinctive public health benefits, exposure reduction programs also reduce health care costs. X-ray examinations, as we extrapolate the number to this past year, using data from 1964 and 1970, as I described, cost nearly $6.5 billion. That is about 4.5 percent of the national health care bill.

Reducing exposure will save costs, of course, in two ways: There will be immediate savings because fewer exams are ordered or because fewer repeat films are taken, or because exposure is better limited and there will also be a longer term saving by preventing future ill health in the form of long deferred genetic damage, or long deferred cancers.

As we calculate them, the ratios of these savings are about a little less than 4 to 1. That is, if you avoid an exposure today that isn't necessary to produce a positive short-term health benefit, you save a direct cost equivalent to $4 and you get another $1 or a little more than $1 in terms of the deferred health benefit from avoided cancers and genetic damage.

Let me just talk about the cost-saving features of a couple of programs. If 10 percent of films are repeated for poor image quality, and if we can achieve our pilot program goal on a national basis, the short-term saving in film alone is $130 million a year.

The largest potential saving is from ordering unneeded exams. The studies done on skull, barium enema and upper GI exams suggest that 40-percent, 10-percent, and 19-percent reductions respectively are possible. Other estimates range from 10 to 40 percent. An overall estimate made by a number of people is that 30 percent are unnecessary; and if that is right—and we could argue 10 percent either way—but if that is right, the national potential available for saving is $2 billion annually in the short-term costs; $500 million in the long-term costs.

Again, calculated in terms of the long-term deferred costs alone, if it is correct—this is using a National Academy of Sciences' figure of $100 in deferred health costs per rem avoided—the X-ray standard itself, which is in place now, will save about $200 million in deferred costs for the machines manufactured in 1978 alone.

In summary, Mr. Chairman, we think we are administering an innovative program that has been successful so far in curtailing exposure of the American public to radiation levels commensurate with the expected benefits. We think our present and future responsibilities are as follows:

First, we want to continue to insure compliance with existing regulatory standards to promote widespread adoption of voluntary guidance and to increase professional education on the prudent use of medical radiation.

Second, we must keep abreast of the emerging technologies and their associated health risks through research and actively encourage these technological developments which improve diagnostic information and reduce patient exposure.

Finally, we have to increase the awareness of consumers and of providers concerning the risks and benefits of radiation and encourage their participation in agency programs and policy-setting activities.

That is the end of my statement, Mr. Chairman. We will be happy to respond to questions from the subcommittee.

[Testimony resumes on p. 295.]

[Dr. Kennedy's prepared statement follows:]

STATEMENT
BY
DONALD KENNEDY
COMMISSIONER
FOOD AND DRUG ADMINISTRATION
PUBLIC HEALTH SERVICE
DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Mr. Chairman:

In the ten years since you set in motion the events that led to enactment of Public Law 90-602, the Radiation Control for Health and Safety Act of 1968, the Food and Drug Administration (FDA) has made significant progress in developing a nationwide program to protect the public from excessive exposure to various forms of electronic product radiation.

It is a pleasant task, therefore, to acknowledge your foresight and our appreciation for the essential role you have played in the establishment of our radiation protection program. I want to describe today how we are using P.L. 90-602 to accomplish the goals envisioned by it for medical radiation and how we are using it to make a difference in the Nation's health care system.

Appearing with me today is Mr. John C. Villforth, Director of the FDA's Bureau of Radiological Health (BRH)

AN ASSESSMENT OF RADIATION HAZARDS: PAST AND PRESENT

I think it would be useful to begin by pointing out that the proliferation of radiation-emitting products over the last decade has raised the potential for human exposure.

Let me briefly sketch the contemporary situation regarding medical and dental x-ray exposure. Approximately 145,000 dental x-ray machines are now being used in 84 million x-ray procedures yearly, and about 125,000 medical x-ray machines are used in about 157 million procedures. Of the 270,000 dental and medical machines in use, 19 percent are complete x-ray systems manufactured and sold after

August 1, 1974, the effective date of FDA's performance standard. About two-thirds of medical x-ray examinations occur in hospitals, with the remainder taking place in private physicians' offices, group practices, and health agencies. Between 110,000 and 170,000 persons operate medical x-ray equipment in the United States. Of these, approximately 80,000 are certified or licensed to practice.

There is some evidence that the actual exposure people are receiving from medical sources may also be on the increase, simply because of the increased number of medical radiologic procedures now being performed. For example:

-- Two FDA-conducted national surveys of x-ray use showed that the annual number of x-ray examinations in the United States increased 24 percent between 1964 and 1970, from 173 million to 212 million. The cost of these household-based surveys has made it prohibitive to continue them. However, we can derive a rough estimate of today's x-ray usage by extrapolating from the 1964 and 1970 data. According to this calculation, approximately 241 million examinations would have been performed last year.

-- A further increase in the overall number of radiologic examinations, and possibly in the average radiation exposure per examination, may be witnessed as a result of the introduction of computed tomography (CT) scanners in the United States in 1973. Already, approximately 700 CT scanners are being used on about 2 million patients per year.

-- Mammography has also contributed to increased exposure (from more X rays per person as well as more individuals being exposed) over a short period of time. This procedure, in which relatively large amounts of radiation are delivered to a particularly radiosensitive tissue, was scarcely used as recently as 15 years ago. It is now being performed on approximately 2 million women in the United States annually.

FDA'S RADIATION PROTECTION STRATEGY

The FDA has and continues to base its radiation control program on assuring the safety of radiation-emitting devices and on encouraging prudent radiation-use practices. Our program is divided into various functional components, in which we:

(1) study biological effects of radiation;
(2) conduct research on improving radiation measurements and the equipment used to obtain them.
(3) establish regulatory performance standards and perform associated surveillance and compliance activities;
(4) issue recommendations for good radiation-use practices;
(5) educate the general public and train professionals and paraprofessionals; and,
(6) participate in cooperative programs with Federal and State agencies.

I would like at this point to submit for the record a report entitled, "The Bureau of Radiological Health -- A Look at FDA's Program to Protect the American Consumer from Radiation," which highlights the achievements of FDA in the field of radiation protection.

In discussing our radiation protection activities, it is important to distinguish between regulation and recommendation--two distinct and complementary approaches used by FDA to reduce radiation exposure.

Regulation is used to assure that radiation-emitting products are safe and effective. The Agency develops and promulgates regulatory product performance standards which are imposed on manufacturers under authorities contained in P.L. 90-602. With the Medical Device Amendments of 1976 (Public Law 94-295), our authority over products in the total x-ray system has been broadened to include such essential elements as x-ray film processing equipment, which have a significant effect on both the quality of the radiograph and the exposure of the patient. I will later describe in some detail our performance standard for diagnostic x-ray machines. We are also considering standards for radiation therapy and ultrasound devices. Although we are highlighting today the use of x radiation in medical applications, I also want to mention that we have established and are actively enforcing regulatory standards for the nonmedical applications of such products as television receivers, cold cathode gas discharge tubes, microwave ovens, x-ray baggage inspection systems, cabinet x-ray machines, and laser products.

Voluntary recommendations, by contrast, are directed at improving x-ray usage practices. We selected the voluntary approach in this area for two reasons. First, issues of medical radiation efficacy and the many techniques which can be employed during x-ray examinations are complex, and good practices tend to evolve over time. Sometimes, therefore, regulatory action in this area can be inappropriate and serve to inhibit medical judgment and the development of new techniques.

Second, P.L. 90-602--like the other laws under which Federal health regulation is carried out--does not authorize us to regulate medical practice. Issues for which recommendations are either in effect, or are currently being developed, include the use of gonad shielding, X rays during pregnancy, radiation treatment for benign diseases, mammography screening, the use of mass chest x-ray screening, x-ray technologist qualifications, and exposure/technique guides for certain x-ray procedures.

I would now like to describe a few of the mutually interdependent and supportive activities which we undertake in dealing with the medical radiation problem.

FDA'S BIOLOGICAL RESEARCH PROGRAM

FDA's concern over the increased use of diagnostic x radiation relates to the potential of low-level radiation exposure for producing adverse effects. Biological research provides a scientific basis for our regulatory and voluntary initiatives; only by understanding the hazards and being able to quantitate the risks from various kinds and doses of radiation can we set sensible program priorities.

The Agency's Bureau of Radiological Health contributes to bio-effects research on the consequences of low-level radiation exposure with a program of experimental and epidemiologic studies conducted through grants, contracts, and intramural research. Let me summarize some of the findings of this research that have direct health implications.

Prenatal Exposure

Irradiation during prenatal development can evoke a variety of biological effects. For example, experimental research in rodents has established that gross visible defects are possible from radiation exposures in the range of 5 to 12 rads during early pregnancy. Many of these defects involve faulty development of the central nervous system. Later in pregnancy, radiation exposure can affect behavior, learning, and coordination. Other experimental radiation effects include interference with expression of genetic information, and retarded growth and development.

Another effect of radiation in utero is carcinogenesis. In humans, the largest and most important study is the Oxford Survey of Childhood Cancer, directed by Dr. Alice Stewart, who testified in February before this Subcommittee. This study, partly funded by FDA, has investigated all leukemia and other cancer deaths in children born in Great Britain from 1953-1975; it now contains records of over 10,000 cancer deaths and an equal number of matched controls. This was the first study to indicate that prenatal exposure to diagnostic X rays, at doses estimated to be in the range of 0.5 to 2 rads, was associated with an increased risk of leukemia and other cancers in children. The study has been a source of substantial controversy, in part because no carcinogenic effect was observed in another study among those exposed prenatally to atomic bomb radiation in Japan. The leukemia findings from irradiation during the third trimester are now generally accepted, as a result both of reanalysis of earlier data and of findings in epidemiologic studies conducted at Harvard and The Johns Hopkins universities. Reports of an increased risk of leukemia from radiation exposure earlier in pregnancy, and of other cancers, are still a source of controversy--particularly in view of the absence of supporting evidence from animal studies.

Such evidence may come from a study we initiated in 1962 in collaboration with Colorado State University to conduct a lifetime evaluation of beagle dogs--whose sensitivity makes them especially appropriate animal models. The animals received 16 or 84 rads of gamma radiation during prenatal or early postnatal development. The study, which has cost approximately $14.5 million thus far, has, over the years, used a total of 1,680 dogs, of which 360 have been nonirradiated controls. Although we are only midway through the study, we already have observed excess cancers in irradiated animals. To date 23 dogs have died of malignancies. Of this number, 5 were in the low-dose group and 16 were in the high-dose group. The other two dogs were in the control group. Several malignant lymphomas were found among the irradiated groups. When the study is completed, it may provide a rationale for the epidemiological observations of radiation-induced cancers in children and provide a more quantitative estimate of risk. This experimental research and the epidemiologic studies of Dr. Stewart and others on the effects of prenatal radiation has helped to provide the basis for an FDA recommendation on the use of diagnostic X rays during pregnancy.

Thyroid Exposure

Another example of our research into the link between radiation exposure and adverse health effects concerns thyroid cancer. Two followup studies of children given x-ray treatments of the scalp for ringworm (tinea capitis), one at New York University and the other at Sheba Medical Center in Israel, have been supported by FDA. The Israeli study showed that the risk of thyroid cancer was increased more than four-fold at doses of 6 to 9 rads, and that the risk was significantly greater for children exposed under the age of six years than for older children. The latent period for the development of malignant neoplasms of the thyroid ranged from 5 to 21 years during the 25-year period of observation. The demonstration of increased risk of thyroid cancer at low x-ray doses in children has increased our concern about the consequences of certain diagnostic procedures. In part because of this concern, we are developing a recommendation on the use of iodine-123 as a substitute for iodine-131 as a thyroid diagnostic agent, because it delivers less radiation exposure to this organ. FDA has also cooperated with the National Academy of Sciences (NAS) in developing general recommendations on the use of radiation therapy for benign diseases, and we are now formulating more specifc guidance concerning those uncommon medical situations in which this form of treatment may still be justified.

Mammography Exposure

The FDA has sponsored studies of other radiation-induced cancers, including breast cancer. One of our collaborative studies at Harvard University showed an increased risk of breast cancer for 10 to 40 or more years after radiation exposure. The patients in the study had been exposed to multiple fluoroscopies in lung collapse therapy for tuberculosis. Another supported study at the University of Rochester showed an increased risk of breast cancer after x-ray treatment for mastitis.

These and other data were used by FDA in a mathematical model to estimate risks and benefits associated with mammography. The model showed that mammographic screening, in conjunction with physical examination, provided relatively more benefit than risk for asymptomatic women over the age of 50. Among asymptomatic women under the age of 50, the risks outweighed the demonstrated benefits. Our analysis was one of several used by the National Cancer Institute's (NCI) Consensus Panel on Breast Cancer Screening in its development of guidelines for the NCI/ACS Breast Cancer Detection Demonstration Projects. FDA is using this analysis to implement dose reduction techniques for mammography, and to support forthcoming national guidance for mammographic screening.

These are some examples of our efforts to provide new data which will allow for a more thorough understanding of the consequences of exposure to radiation. The findings of our research have formed part of the data base considered by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) in developing the risk assessments recently published in the report, "Sources and Effects of Ionizing Radiation, UNSCEAR 1977 Report to the General Assembly." We anticipate that our research will also be considered by the National Academy of Sciences in its soon-to-be-released report on the biological effects of ionizing radiation.

I would like to submit for the record a document which summarizes our biological effects research activities in the area of ionizing radiation.

FDA's PERFORMANCE STANDARD FOR MEDICAL AND DENTAL X-RAY EQUIPMENT

Introduction

As I stated earlier, P.L. 90-602 gives the Agency a clear legislative mandate to establish performance standards for radiation-emitting electronic products. One of the most important standards promulgated thus far has been that for diagnostic medical and dental x-ray units, which applies to all systems and components manufactured after August 1, 1974. The standard covers complete x-ray systems as well as individual components that may or may not be installed with other certified components. Examples of complete systems include dental radiographic units, general purpose radiographic and fluoroscopic units, both mobile and stationary, and specialized systems such as mammographic units. Eleven separate components are covered by the standard, including x-ray controls, tables, and x-ray beam limiting devices. Because these components are sold separately and each is subject to certain requirements of the standard, these are actually the equivalent of 11 separate performance standards.

At this time, 158 factory-based manufacturers, both domestic and foreign, are producing more than 5,000 components covered by the standard. Each manufacturer must conduct a testing and quality control program that assures that all components will comply with the standard, and must apply a certification label to each component. In addition, specific regulations are directed at the 2,100 assemblers of these x-ray systems and components, since the proper installation of the equipment determines to a large extent whether a system or component complies with the performance standard.

The FDA enforces this standard through a review of reports submitted by manufacturers, plant inspections, laboratory testing, and field testing.

Report Review

The reports submitted by manufacturers and reviewed by BRH describe the testing and quality control program under which a factory-based manufacturer produces the product to comply with the performance standard. These reports also describe how the product is designed to meet the standard, and include user, assembly, and maintenance instructions provided by the manufacturer. An initial report must be submitted to the BRH before the product is introduced into commerce. Subsequent model change and annual reports update and summarize the testing program.

From a review of the reports, it is possible to identify items of noncompliance and questionable areas of a testing program. This information is then used by itself or in combination with the results of field tests, lab tests, or a plant inspection to officially notify the manufacturer of a noncompliance. As an example, from reviewing one firm's initial report and the results of field tests, the Agency declared noncompliance against a manufacturer for violating eight requirements of the standard relating to the x-ray beam limiting component. The noncompliance related primarily to excessive field size, which results in unnecessary exposure to the patient and, in the case of field sizes in excess of the primary protective barrier, to operators of the equipment. It was estimated that the malfunctioning positive beam limitation device could cause the x-ray beam to be 50 percent or more larger than the size of the film. The manufacturer is currently conducting a corrective action program for the approximately 2,000 components.

Unfortunately, FDA has not been able to review all reports that have been submitted. This problem was recognized by the General Accounting Office in its report of November 24, 1976; at that time, 35 percent of the reports received had been evaluated. As a result of additional resources, the current level of reports reviewed has increased to 50 percent. One of the additional steps we are taking to reduce this problem is a revision of the manufacturer's reporting guide which we believe will both simplify and improve the reports and expedite the Agency review process.

Plant Inspections

Inspections of domestic and overseas factory-based manufacturers are conducted to review closely the testing program described by the manufacturer in his report and to observe the instrumentation that the manufacturer uses to assure compliance with the standard. These inspections are extremely valuable, both in enforcing compliance with the regulations and in providing assurance that the manufacturer has a full understanding of the requirements. To date, we have inspected every domestic and foreign manufacturer at least once. An example of the value of these inspections occurred during a visit to one overseas manufacturer. We observed that a mammographic unit had no provision for adjustment of the x-ray field to the image receptor. After notification by FDA, the manufacturer changed the product design to include a mechanical linkage between the x-ray tube housing and the image receptor, and also installed it on the units already in use.

Laboratory Testing

Laboratory testing is by far the most comprehensive compliance testing performed by FDA; it is conducted to thoroughly measure the compliance of a manufacturer's product with the performance standard. This testing is performed on self-contained systems and components small enough to be sampled and laboratory tested, such as dental x-ray units and mobile medical radiographic systems. One case in which laboratory testing proved its value involved defective dental x-ray units. Following a report by a State Health department that one type of dental machine may not have been performing as it should, laboratory tests disclosed that the actual measured kVp was in the range of 40 kVp at 110 volts, even though these machines were advertised and sold as 60 kVp units. At 40 kVp, the units would have delivered five times more skin exposure than they would at 60 kVp. The FDA required correction of approximately 1,200 of these dental machines, involving 9 importers of either identical or similar units.

Field Testing

Field testing of medical and dental x-ray equipment is performed in hospitals, clinics, and doctors' offices and provides a means of measuring compliance of both the factory-based manufacturer and the assembler. For the factory-based manufacturer, it allows for our testing of components and systems that cannot be brought to our laboratories. For the assembler, it is the primary means by which we determine if the equipment is properly installed. Field testing is conducted by Agency personnel and through contracts with 22 State radiation control agencies. Since August 1974, about 15 percent of all certified x-ray machines have been tested under this program. Approximately 60 percent of these were tested within 6 months following installation and 94 percent within one year of installation. The results of this testing have indicated a high rate of noncompliance, in part, we believe, because the standard is still relatively new and also because its technical requirements are very complex. Since individual units are being corrected on a one-on-one basis with communication between FDA and the involved assembler, this program is being expanded with an additional $400,000 scheduled for new State compliance contracts beginning later this fall. These contracts will be monitored by specially trained FDA personnel who will also perform additional testing.

One example of a recall initiated because of field compliance testing involved a special purpose urology unit. It was observed during compliance testing, that the x-ray timer malfunctioned so that a repeat exposure occurred inadvertently. There was about a one-second time delay between repeat exposures and an alert technologist could prevent double exposures by quickly releasing the exposure button. One of the technologists interviewed, however, indicated that this was learned only after some film retakes were required, resulting in unnecessary exposure to the patient. The company engineers determined that the double exposure resulted from a faulty timer circuit board, and the timers were replaced with a different model.

Since the standard became effective (August 1974), factory-based manufacturers have conducted 72 recalls of medical and dental x-ray units, involving more than 38,000 noncompliance products.

In addition to those recalls which were required because of the failure of equipment to comply with the performance standard, there have been 26 recalls of medical and dental x-ray systems involving more than 35,000 products under the provisions of P.L. 90-602 related to defective products. These provisions apply to all products manufactured since October 18, 1968, and provide a mechanism to control unnecessary exposure from equipment manufactured prior to the effective date of the performance standard and also to cover any radiation safety items that may not have been included in the performance standard. An example of this type of action is a case in which a component failed, so that the timer control on certain x-ray machines did not automatically terminate x-ray exposures. Should the control have failed during a patient examination, the estimated unnecessary exposure could have been from 3 to 5 times that from a normal procedure, up to (under very worst case conditions) 79 R. Even though the number of actual failures was small and it was not possible to accurately predict the future failure rate, the manufacturer was required to notify purchasers and modify the control circuitry in all 961 units.

The performance standard required many major changes in the design of x-ray machines and the testing and quality control programs under which they are manufactured. This has sometimes accelerated technological innovation in the medical x-ray field. For example, positive beam limitation (PBL) was initially developed in our laboratories during the late 1960's, but was not commercially available. FDA required PBL in its diagnostic x-ray performance standard, and, as a result, this feature is now a widely available tool to protect patients. The standard has also forced the Agency to initiate in-house development of new testing equipment, concepts, and procedures, which are now used by manufacturers in their own plant and field testing programs.

The standard has also meant new requirements upon the assemblers of these products. Assemblers must now closely follow the manufacturer's instructions for installation and to certify that they have done so. Our enforcement methods have been directed at improving manufacturer testing programs in an attempt to prevent noncompliance to assure that ultimately all products manufactured and assembled will comply with the standard. We are concentrating our efforts at this time on those factory-based manufacturer test programs which our field testing has shown to be most in need of change. These changes often include improvements in the quality of instructions provided to the assembler of the equipment. Continuing efforts are also directed at educating assemblers in the important role that they play in putting together a compliant system.

The standard has been changed since it became effective in 1974 and will continue to change in the future as advances in health technology necessitate the regulation of new radiation products which represent a potential health risk. Such is the case for computed tomography (CT) systems, which were not in use when the x-ray standard was being developed. Although the general provisions of the standard apply to CT systems, specific amendments applicable for these products are needed and we expect to publish a proposed regulation early next year.

NON-REGULATORY PROGRAMS

Even the most effective regulation of x-ray equipment cannot guarantee that patients will receive a minimum of exposure during x-ray examinations, any more than standards for automobiles can assure safety in driving. For this reason, FDA has programs to improve the practices of those who prescribe X rays and those who operate the equipment. These programs consist essentially of establishing recommendations for good radiation practices and educating health personnel and consumers.

Quality Assurance

One major source of unnecessary patient exposure from diagnostic x rays is failure of the operator to use good practices. This problem is being addressed in several voluntary quality assurance programs conducted by FDA in conjunction with State and municipal radiation control agencies.

Two the these joint projects between FDA and the States have demonstrated in particular that they can effectively reduce x-ray exposure. One is a dental quality assurance program known by the acronym "DENT," or "Dental Exposure Normalization Technique," and the other is a mammography program known as "BENT," or "Breast Exposure: Nationwide Trends." In both cases, these FDA designed programs enable State and municipal radiation control agencies to quickly identify x-ray facilities where unusually high exposures are taking place. This is accomplished by mailing special cards, which were developed by FDA, to x-ray offices and hospitals. The instructions tell the x-ray operator to expose the card as would normally be done in a dental or mammographic x-ray procedure. The cards, which contain an inexpensive radiation measuring device, are mailed back to the State agency, where they are read. The next step is for the State radiation protection personnel to visit the high exposure facilities to help identify the problem and to suggest improvements in x-ray techniques which can lower exposure and improve diagnostic quality. We have found that the chief problem in high exposure dental facilities has been poor film processing. In the 41 State, Federal, and municipal agencies which have evaluated the dental program, a 40 percent average reduction in dental x-ray exposure to patients has been demonstrated. We expect that the mammography program, now in 42 States, will yield similar results.

I should mention here that Secretary Califano has expressed his personal interest in these programs by writing to all Governors and urging them to participate in "BENT" and DENT." This has had a beneficial effect in increasing the awareness of the importance of these programs.

Another potential exposure saving lies in the reduction of repeat films necessitated by poor techniques. Published estimates indicate that about 5 to 10 percent of diagnostic x-ray films must be repeated; a substantial number of these repeats are avoidable through improved quality assurance practices in x-ray facilities. We are promoting the establishment of such quality assurance programs by a recently proposed Agency recommendation. To demonstrate the value of adequate quality assurance in hospitals, we pilot-tested a system to monitor x-ray film processors at our Baltimore Public Health Service (PHS) hospital. By improving film processing alone, we demonstrated a 30 percent reduction in retakes. Studies conducted by film manufacturers in other hospitals have substantiated this effect. We are now expanding the system to the rest of the PHS hospitals, and are working on a standard protocol for processor quality assurance procedures, which can be applied to all hospitals.

An important aspect of our program to improve people's x-ray practices is to develop and distribute continuing educational materials. For example, we are producing a series of training packages designed to teach such things as the use of gonad shielding and proper x-ray beam restriction to x-ray technologists. The messages are in the form of slides, audio-tapes, and workbooks. These particular packages are being used by approximately 10,000 student and practicing technologists each year, and we believe that they will have a positive effect in improving operator performance.

Radiologic Efficacy

Another major source of unnecessary exposure lies in the ordering of unneeded x-ray examinations. Physicians are understandably concerned about the professional and medico-legal consequences should they fail to make an adequate diagnosis. This can cause them to prescribe x-ray procedures whose results do not measurably alter patient management or outcome. A major obstacle in dealing with the broad issue of unnecessary x-ray examinations is the lack of scientific efficacy data that could be used to guide physicians (and the legal profession) about when X rays are warranted and when they are not.

We have made a start in dealing with this problem. An FDA-supported project in a large Washington State hospital, involving over 5,000 patients, has demonstrated a 40 percent reduction in emergency room skull X rays for trauma through the use of definitive criteria for ordering these X rays. Should we be able to expand this project to achieve national coverage, and should we be able to develop x-ray ordering criteria for other examinations, this would result in a significant reduction in population exposure to x radiation.

Another FDA program aimed at x-ray ordering practices will make physicians more aware of the need to consider pregnancy status in deciding whether to order, modify, or forego abdominal x-ray examinations for women of child-bearing age.

Consumer Education

The problem of ascertaining the pregnancy status of a young woman before prescribing an abdominal x-ray examination exemplifies the importance of good communication between the patient and the health practitioner. FDA is committed to improving this communication by educating consumers about the benefits and risks of diagnostic X rays, and by teaching them what they can do to reduce unnecessary exposure. As an example of this commitment, we are distributing a poster in collaboration with the American College of Obstetricians and Gynecologists, alerting women to tell their doctors about possible pregnancy. We believe that by volunteering needed information and by asking the right questions, consumers can reduce unnecessary exposure to themselves and their families. As consumers become better educated, and as they learn more about radiation protection, they will become increasingly equipped to contribute to the careful and judicious use of X rays.

One of our consumer education efforts is a wallet size x-ray record card. It enables patients to keep track of their x-ray examinations and to inform physicians about previous examinations. The results of earlier X rays can be diagnostically useful, and using the card may also help to avoid repeat procedures. We have similar educational programs which teach consumers to ask physicians and technologists about using gonad shields, and which caution patients and parents against insisting on X rays when they may not be needed.

We are aware that educating people about the benefits and risks of medical radiation is not an easy task. Our goal is more complex than the simple message of an antismoking campaign, in which people are warned to completely refrain from a practice which is hazardous and which has no significant benefit. Consumers must understand that medical radiation exposure, when used properly, carries with it tremendous health benefits. If we were to create such anxiety about radiation dangers that people refused needed x-ray examinations, this would surely result in more harm than good.

INTERAGENCY RELATIONSHIPS

I know that the Subcommittee is deeply concerned that Federal radiation responsibilities, which are divided among several agencies, be managed and coordinated responsibly so that the American public is adequately protected. We agree that coordination of Federal radiation protection activities is vital to the control of unnecessary radiation exposure and maximization of Federal resources and expertise. I would like to assure the Subcommittee that FDA and its sister agencies with radiation responsibilities are making concerted efforts to coordinate programs, share resources, and prepare interagency problem analyses and program strategies. The object of this coordination is to avoid duplication of effort or jurisdictional dispute, and to provide comprehensive coverage for all radiation hazard problems.

The Agency has effected this kind of interagency cooperation through an array of formal collaborative efforts, which include 29 Memoranda of Understanding and Interagency Agreements with Federal agencies both within and outside the Department; a list of these is attached to my testimony. An example of this collaboration is the support provided by the National Cancer Institute for our "BENT" mammography quality assurance program, which has enabled us to expand State participation more quickly than would have otherwise been possible.

Proper illustration of these interagency efforts is our Memorandum of Understanding with the Environmental Protection Agency on the issue of medical radiation guidance for Federal facilities. This guidance was approved by the President on February 26, 1978. The Assistant Secretary for Health has directed FDA to aid in the implementation of the President's directive in Federal institutions and to explore utilization of the recommendations across a broad spectrum of U.S. health care facilities. FDA also works with the National Bureau of Standards on the various aspects of instrumentation and measurement techniques, and has participated with the Nuclear Regulatory Commission (NRC) in the development of a standard for the accurate interpretation of occupation radiation doses.

Coordination of radiation protection activities is not limited to the Federal sector. FDA has a close working relationship with State and local radiation control agencies. This alliance with the States has provided us with an implementation vehicle for both our regulatory enforcement efforts and voluntary exposure reduction programs, such as "DENT" and "BENT." We view this partnership as essential and effective toward assuring radiation protection at the "grass roots" level. This relationship also helps to ensure compatibility with Federal radiation requirements and, with the cooperation of NRC, EPA, and OSHA has produced model regulations which provide States with an authoritative guide for regulatory codes covering all sources of ionizing radiation. FDA has joined with the States, the EPA and NRC in sponsoring the National Conference of Radiation Control Program Directors, which serves as a forum for joint Federal-State action on various radiation problems.

COST CONTAINMENT CONSIDERATIONS

A beneficial byproduct of FDA's various programs to reduce radiation exposure is a concomitant reduction in health care costs. X-ray examinations presently account for approximately $6.3 billion annually in health care expenditures, and we believe that this can be significantly reduced through our programs. Lessening unnecessary x-ray exposure can yield two cost containment benefits. The first is an immediate saving if fewer unnecessary examinations are ordered, or if fewer repeat films are needed. The second is an accrued saving through the prevention of future radiation-inducted health problems, e.g., cancers and genetic disorders.

With respect to the immediate saving from reducing repeat films, a variety of published estimates agree that about 10 percent of films are repeated because of poor quality. Approximately one-third of these should be avoidable through the kinds of quality assurance programs for x-ray facilities which we are developing. If this is the case, the potential short-term saving in the cost of extra film, materials and labor is about $130 million per year.

By far the largest potential saving in immediate radiology costs is related to the ordering of x-ray examinations which do not contribute to the patient's medical management. These X rays are ordered in part because of a lack of scientifically developed criteria on when X rays are useful and when they are not. Other reasons include an inadequate patient history, medico-legal pressures, or patients insisting on X rays. An accurate estimate of the proportion of today's x-ray examinations which may not be needed for satisfactory medical management is not available, but we have used 30 percent as a reasonable approximation, based on a variety of published studies. For example, studies testing the feasibility of using definitive x-ray ordering criteria for skull, barium enema, and upper GI examinations have shown that it is possible to reduce their frequency by 40 percent, 10 percent, and 19 percent respectively, without adverse effects on patient care. Concerning the problem of "medico-legal" examinations, the American College of Radiology has estimated that 6 percent of emergency room X rays may be ordered for this reason, while the president of Blue Shield of California has indicated that between 30 and 40 percent of x-ray procedures are ordered for defensive reasons. Since studies of these kinds have generally been conducted at individual institutions and in most cases apply to only specific types of x-ray procedures, our 30 percent overall estimate is necessarily a rough approximation.

Using the 30 percent estimate, it can be seen that the potential saving which could be realized if better x-ray ordering criteria were developed and used for all examinations would be on the order of $2 billion annually (approximately one-third of the present cost of x-ray examinations).

Recall that the second type of saving is in the reduction of future health care costs through preventing radiation-induced ill health. Future cancers or genetic effects result in long-term costs to society, both in treatment and in lost wages and productivity. We have reviewed the range of estimates in the literature for the future health cost of radiation exposure (including a projection by the National Academy of Sciences of $19-190 per rem and one by the Nuclear Regulatory Commission of $1,000 per rem) and, in order to have a means of assessing the impact of our actions, we decided to use the assumption that each rem of radiation dose avoided will result in a long-term saving in health care costs of $100, measured in today's dollars. On this basis, it can be estimated that for those x-ray machines manufactured in 1978 alone, the radiation exposure reduction brought about by our diagnostic x-ray performance standard will result in future health care savings of about $200 million.

For the sake of brevity, we have chosen only a few examples to illustrate the cost containment potential of our radiation exposure reduction programs. Similar benefits can be calculated for our other activities which reduce population exposure.

SUMMARY

Mr. Chairman, we believe that we are administering an innovative program which has been successful thus far in curtailing exposure of the American public to radiation levels commensurate with the expected benefits. We view our present and future responsibilities as follows:

- -- We must continue to ensure compliance with existing regulatory standards, to promote widespread adoption of voluntary guidance, and to increase professional education on the prudent use of medical radiation.
- -- We must keep abreast of emerging technologies and their associated health risks through research, and actively encourage those technological developments which improve diagnostic information and reduce patient exposure.
- -- We must increase the awareness of consumers concerning risks and benefits of radiation and encourage their participation in Agency policy-setting activities.

This concludes my statement Mr. Chairman. We would be happy to respond to any questions you or members of the Subcommittee might have.

Mr. ROGERS. Let me just ask one question before I call on the other members.

If 30 percent of exposure is unnecessary—and I think you have stated you feel that is probably an appropriate figure—what is FDA's assessment of the health effects of this unnecessary exposure and the number of excess deaths, the number of excess diseases, the amount of excess disease and genetic damage? Or have these figures been set?

Dr. KENNEDY. I think there are such figures. I am not sure whether we have supplied them actually to the subcommittee or not.

Let me begin by saying that the Committee on the Biological Effects of Ionizing Radiation says the exposure to the ambient level in the United States, a tenth of a rem, causes somewhere between 2,000 and 9,000 excess cancer deaths per year.

As you know, we apply a linear dose response relationship to radiation. That allows you to get an approximation of the amount that would be associated with an exposure, an unnecessary exposure of a particular magnitude.

What you would have to do—and I bet John is trying to do the numbers at the table here, we may be able to give them to you now, or we may have to given them to you later—is to take that proportion and to try to decide what the annualized cancer risk is that would be associated with 30 percent of 241 million X-ray examinations, which is the estimated number per year.

We will do that and supply you with that number.

[The following information was received for the record:]

ASSESSMENT OF THE HEALTH EFFECTS FROM UNNECESSARY X-RAY EXAMINATIONS

To assess the exact amount of ill-health associated with unnecessary X-ray examinations is not possible with any reasonable degree of accuracy. Thirty percent is a composite figure, derived from a number of published studies in the medical literature. We do not know whether the proportion of various kinds of X-ray examinations in this 30 percent avoidable segment is the same as the proportion in the 70 percent "necessary" segment. The literature references, upon which the 30 percent estimate was based were silent both with respect to the types of X-ray procedures involved, as well as the corresponding X-ray doses and health effects. Since various kinds of X-ray procedures expose different parts of the body and different critical organs to varying amounts of radiation, it is not possible to precisely calculate the radiation dose which would be saved by eliminating the unnecessary 30 percent. Therefore, without this data, the number of cases of adverse health effects (cancers, leukemia cases, genetic effects, etc.) which would be caused by the unnecessary 30 percent of X-ray examinations cannot be derived.

Mr. ROGERS. I think it would be helpful to articulate that so that the public understands and the profession understands the severity of the problem. Until, perhaps, we make that public in terms that everyone can understand, I am not sure the people really can have a full understanding of the significance of the effects of radiation particularly the unnecessary effects.

Dr. KENNEDY. Mr. Chairman, if I might. I don't want to try to wiggle off the hook here, but one of the difficulties is that although there is some agreement that 30 percent is not a bad midpoint figure for excess exposures, agreement is less easy to get about which procedures are the ones that are most often unnecessary.

As you well know, different procedures yield different amounts of radiation exposure. It is one thing to be able to say that if we could reduce all exposures by 10 percent, we could calculate a quite exact number for you. But to say we reduce the number of exposures by 30 percent, it matters which ones you eliminate. So 30 percent is already a sort of rough cut average figure, and any figure we have you on deferred cases would be even more rough cut and I think we would have to treat it with a good deal of caution.

Mr. ROGERS. Yes; I presume so.

I would have thought this would have already been done and figured out.

Dr. KENNEDY. I think it was not done only because we felt that the range would be so wide that it might not be terribly informative, Mr. Chairman.

Mr. ROGERS. Mr. Carter.

Mr. CARTER. Thank you, Mr. Chairman.

Dr. Kennedy, do you strongly approve of the use of radiopharmaceuticals in diagnoses?

Dr. KENNEDY. Do I strongly approve?

Mr. CARTER. Yes, sir.

Dr. KENNEDY. I know they are terribly valuable, irreplaceable in most situations, and I only assume that their benefits vastly exceed their risks.

Mr. CARTER. Vastly exceed.

Has there been any increase in thyroid cancer as a result of the use of radioactive iodine-123?

Dr. KENNEDY. I am not really able to answer that question, Dr. Carter.

Mr. CARTER. Why do you suggest we change from the use of iodine-123 to iodine-131?

Dr. KENNEDY. Well, the recommendation for that change results from some studies in which other kinds of radiation exposure demonstrated an increase in thyroid cancer and——

Mr. Carter. You recommended a change from iodine-123 to iodine-131.

Dr. Kennedy. It is the other way, I think, Dr. Carter, but it doesn't matter. One simply has lower emission.

Mr. Carter. One has lower emission, so you changed to it. Why did you do that?

Dr. Kennedy. Simply because it would produce less exposure and less risk.

Mr. Carter. Then there is some danger?

Dr. Kennedy. There is, unambiguously, a danger from radiation to the thyroid.

Mr. Carter. That is exactly what I wanted you to say. That is the point.

Do you believe in the linear hypothesis?

Dr. Kennedy. As a part of radiation?

Mr. Carter. Yes. Do you think there is a certain point at which cancer mutations occur?

Dr. Kennedy. Do you mean, Dr. Carter, a certain point in the cell?

Mr. Carter. Well, a certain level of exposure.

Dr. Kennedy. Yes.

Mr. Carter. You do? You think there is a certain level of millirads at which cancer mutations are caused?

Dr. Kennedy. No. I thought you meant a certain location at which radiation exerted its mutagenic action. By linear, I mean linear; that is, a single hit model.

Mr. Carter. Well, by that hypothesis with increasing amounts of radiation, you get more and more damaging effects; is that not correct?

Dr. Kennedy. That's correct.

Mr. Carter. We heard testimony yesterday that from 30 to 50 percent of all X-ray equipment, must be returned to the factory shipping door from the ultimate destination because of failure to meet standards of the Bureau of Radiological Health; is that correct?

Dr. Kennedy. I believe that 30 percent is our figure. Is that not right?

Mr. Carter. Thirty to fifty percent, I believe. An average would be 40 percent.

Dr. Kennedy. The figure we have is 30, Dr. Carter.

Mr. Carter. The Senate hearing record states 30 to 50 percent.

Dr. Kennedy. Whose testimony was that?

Mr. Carter. It came from page 21 of the radiation hearings of the Committee of Commerce and Science, June 16, 17, 20, and 22, 1977. What sanctions can your bureau impart to assure compliance with equipment standards?

Dr. Kennedy. We have no criminal sanctions. We can tell them to fix the equipment; we can recall the equipment; we can make a fuss. We can sue for an injunction through the courts, and civil penalties.

Mr. Carter. Do you look at the reports before they go out?

Dr. Kennedy. Do we check it with instrumentation?

Mr. Carter. Yes, sir.

Dr. Kennedy. We do not, in most cases, I believe.

Mr. **Carter**. You do not?

Dr. **Kennedy**. Do not.

Mr. **Carter**. Then how do you determine whether the equipment meets your standards and whether you should recall this equipment?

Dr. **Kennedy**. When we visit plants, we look at the quality control data. I suppose that when we actually inspect in plants, we may notice defects in quality control of manufacturing systems and then test——

Mr. **Carter**. Do you do this regularly?

Dr. **Kennedy**. In plants?

Mr. **Carter**. Yes.

Dr. **Kennedy**. Yes, sir.

Mr. **Carter**. I think that is very necessary.

Do you need additional authority to improve compliance with equipment standards to reduce unnecessary exposure of humans to X-rays?

Dr. **Kennedy**. I think it certainly might improve compliance to have some criminal penalties available, as we do in other parts of our law.

I want to be careful, Dr. Carter, because I am not certain that we have encountered particular problems in the past that I can say result from the lightness of the sanctions available to us, but certainly that would make this portion of our law more like the rest.

Mr. **Carter**. How cooperative have the companies been which either manufacture or assemble X-ray equipment in relation to developing a beam which covers the film but no more?

Dr. **Kennedy**. Dr. Carter, can I get some help from my colleague, Mr. Villforth, on that question?

Mr. **Villforth**. The performance standard requires that the manufacturers of general purpose equipment, in order to meet the standard, must certify that they have some concept of positive beam limitation or automatic collimation which locks the X-ray beam to the size of the X-ray film. That is a requirement with the performance standard.

Mr. **Carter**. Would you repeat that?

Mr. **Villforth**. There is a requirement that the manufacturer provide some mechanism, such as positive beam limitation or automatic collimation. We sometimes use these terms interchangeably.

Mr. **Carter**. Is this in effect at the present time? Are you requiring this?

Mr. **Villforth**. Yes, sir, for medical diagnostic X-ray machines.

Mr. **Carter**. I understand a comparative study of mortality and morbidity of radiologists has been supported by your bureau. What is the status of that study?

Dr. **Kennedy**. May Mr. Villforth answer that?

Mr. **Villforth**. The study has been terminated. The funding has been terminated several years ago. The population of physicians, pathologists, and radiologists, the information on those is available in the event we want to reinitiate the study after additional years have gone by for more followup. The termination of the project has not resulted yet—we are in the process of doing this—in the publication of the findings of the previous study. It is still being analyzed, still being reviewed. So we want to find out whether or not there is any effect in the life-shortening or the cause of death between pathologists who do not routinely use radiation and radiologists who do use radiation. That roster of physicians is available for further study and followup in the future as more years pass by.

Mr. CARTER. What is the status of your study now? Did you stop funding of it?

Mr. VILLFORTH. We have stopped the funding of the collection of data. We are in the process of analyzing it and will publish the results.

Mr. CARTER. When did you start this study?

Mr. VILLFORTH. I think the study was started in 1961.

Mr. CARTER. When did you stop funding?

Mr. VILLFORTH. The data collection contract was stopped, I think, 2 years ago.

Mr. CARTER. 1976.

When did you analyze the data?

Mr. VILLFORTH. The data is being analyzed now. It has been analyzed since we stopped the collection phase, which was 2 years ago.

Mr. CARTER. You started the study in 1961 and we don't have any results?

Mr. VILLFORTH. Not of the last study of 1976.

Mr. CARTER. Do we have any preliminary results?

Mr. VILLFORTH. There are some observations.

Mr. CARTER. What are these observations?

Mr. VILLFORTH. There are observations which are about to be published which illustrate that, among other things, that radiologists' families have a higher tendency to get more radiographs than pathologists' families, which would suggest the proximity——

Mr. CARTER. A tendency to get more radiographs?

We want to know about the health effects.

Mr. VILLFORTH. We don't have those results completed.

Mr. CARTER. My, my, my. After 17 years of study you don't have those results? How much money have you put into that study? I would like to know that.

Mr. VILLFORTH. I can give you that for the record. I want to point out the earlier study started in 1961.

Mr. CARTER. And your conclusion is, after 17 years of study, that radiologists' children have more X-rays than pathologists' children; is that correct? That is what you have told me.

Mr. VILLFORTH. That is the result of the recent 1976——

Mr. CARTER. What?

Mr. VILLFORTH. The 1961 data has been published and is available.

Mr. CARTER. Is that all you have concluded? My goodness. I know you have not been there very long. You may be a career man.

Mr. VILLFORTH. Dr. Kennedy has not been there long; I have been there long.

Mr. CARTER. You have been conducting this study for 17 years and you have come up with the fact that radiologists' children have more X-rays. What we would like to know is whether they have more defects when they are born?

Mr. VILLFORTH. The results of the study when it was first published did not show significant effect.

Mr. CARTER. What about the radiologists themselves? Do they have a higher incidence of leukemia or cancer?

Mr. VILLFORTH. As far as the most recent study, we will have to wait for that data to be analyzed.

Mr. CARTER. The study started in 1961. Surely you have a report on that and a little bit of analysis; certainly something by now?

Dr. KENNEDY. Can I make a point here, Dr. Carter?

Mr. CARTER. Yes, sir.

Dr. KENNEDY. It is not uncommon for epidemiological studies of long latent disease not to yield significant results for a long time. I seem to recall that the latency to leukemia is close to 10 years; isn't that right?

Mr. CARTER. I know that; that is true. But we have had this study going on for a long time, and surely something should have been found out by this time other than the fact that radiologists' children have more X-rays than pathologists' children.

Dr. KENNEDY. We will submit what has been published for the record, Dr. Carter. I apologize, but my understanding of it——

[Testimony resumes on p. 313.]

[The following material was received for the record:]

CLARIFICATION OF THE TWO RADIOLOGIST STUDIES

The Radiation Registry of Physicians

The Registry was started at the Johns Hopkins University and in 1968 was taken over by the Bureau of Radiological Health. Its objective was and is to investigate the long term somatic (bodily) and genetic effects in humans of chronic exposure to low levels of ionizing radiation.

Radiologists who have been occupationally exposed to ionizing radiation and a non-exposed comparison group, pathologists, were queried by mail. Two questionnaires have been completed by the same physicians, with a minimum interval of five years. Information collected includes demographic characteristics; occupational, personal, and family radiation exposure; somatic effects of radiation such as injuries, leukemia, and other cancers; and genetic effects such as numbers and sex of children, pregnancy wastage, and congential defects. Project review is provided by a National Academy of Sciences - National Research Council Advisory Committee which is supported by FDA contract.

A descriptive overview of results from the first questionnaire was published in 1971, and although it furnished several suggestive leads, the data at that time were not adequate to draw firm conclusions. The data from the second questionnaire have been compiled, and several papers are being developed. The first of these show that radiologists and their families have a higher frequency of personal medical diagnostic and therapeutic radiological procedures than do pathologists and their families.

A second study is a reanalysis of the sex ratio of the children of male radiologists and pathologists. The first study (1971) showed a higher percentage of male children in radiologists (52% vs. 49%) that was consistent with the hypothesis of radiation-induced dominant lethal mutations on the X chromosome. Preliminary inspection of the results from the second questionnaire failed to confirm this finding, and a more detailed analysis that considers several concomitant variables (age of father, birth order, family size, years in practice of radiology, etc.) is in progress.

Other analyses of these data also in progress include a study of the differences in congenital anomalies and fetal wastage between radiologists and pathologists and a study of the causes of death in the two medical specialties.

Current Trends in Survivorship of Radiologists

The objectives of this study are to determine if radiologists have an increased risk of death from non-specific aging; to compare the risk for radiologists who entered the specialty after newer safety methods were introduced to those who were in practice earlier; and to ascertain if any specific causes of death were increased.

By way of background, in 1965, Drs. Seltser and Sartwell of Johns Hopkins University reported that the death rates of radiologists were higher than those of other physicians specialists for the time period 1935 - 1958. The same relationship existed for cancer, cardiovascular - renal disease and all other causes. The present study which is under the direction of Genevieve M. Matanowski, M.D., Dr. P.H., extended the period of observation through 1969. Data were secured from death certificates and causes of death reported to the American Medical Association.

The study specifically compared members of the Radiological Society of North American, the American College of Physicians (internists) and the American Academy of Ophthalmology and Otolaryngology. The data were analyzed by 10-year-of-birth cohorts with members also grouped according to year of entry into their respective societies. It is noted that Society members in the 1950 -1959 and 1960 - 1969 cohorts have not been in their respective specialties long enough to assess the possible effects of low-level radiation.

The following results relate to the cohorts from 1920 through 1949:

1. Compared to other specialists, there is an excess in mortality rates for all causes for radiologists who entered the specialist societies in 1920 - 1929 and 1930 - 1939, but not for later entries.

2. An excess in cancer mortality among radiologists in comparison with other specialists was found to persist in all cohorts from 1920 through 1949. Leukemia mortality rates were higher among radiologists in the 1920 - 1929 and 1930 - 1939 cohorts, but not in the later cohort. Mortality from lymphoma was higher among radiologists in the 1930 - 1939 and 1940 - 1949 cohorts, but not in the earlier cohort. Mortality from no other site of cancer was consistently higher intwo or more cohorts.

3. The carcinogenic effect of ionizing radiation was not eliminated for the 1940 - 1949 cohort by the decrease in occupational exposure in the first three cohorts, 1920 - 1949. Although cancer death rates were low for radiologists at younger ages in the 1940 - 1949 cohort, these death rates rose sharply in those over 50 years of age and peaked in age group 60 - 64 years. The peak rate for radiologists was about 8 times higher than the rate for ophthamologists. This study documented an occupational hazard for radiologists based on the effects of ionizing radiation. Through papers in professional journals, the radiologists were informed of the increased risk associated with their past experience.

[Reprinted from RADIOLOGY, Vol. 99, No. 3, Pages 559-568, June, 1971.]
Copyrighted 1971 by the Radiological Society of North America, Incorporated

Radiation Registry of Physicians[1]

CHARLOTTE SILVERMAN, M.D. and RAYMOND SELTSER, M.D.

ABSTRACT—Preliminary findings for the original group of approximately 7,900 specialists given a Radiation Registry of Physicians questionnaire are presented. The questionnaire was developed for the purpose of studying the biological effects of prolonged exposure to ionizing radiations among radiologists and comparable specialists. The study population is the total living membership of the American College of Radiology and the College of American Pathologists as of December 1961 and thereafter. The questionnaire furnished information about personal characteristics, possible exposures to ionizing radiations or other health hazards, and reproductive and family histories.

INDEX TERMS: Education • Epidemiology • Radiations, surveys • Radiations, Injurious Effects, as result of diagnostic procedures • Radiations, Injurious Effects, in physicians, radiation personnel, etc. • Radiology and Radiologists

Radiology 99:559-568, June 1971

THE HISTORY of the Radiation Registry dates back to 1959, when an *ad hoc* Committee on the Follow-up Study of Radiologists was convened by the Division of Medical Sciences of the National Academy of Sciences–National Research Council (NAS-NRC). In December 1959, this committee, stimulated by the interest of committee chairman Shields Warren (13), unanimously voted to approve the establishment of registries for collecting data on radiologists and suitable comparison groups as a resource for future studies, recognizing that this was one of the few available means of gaining knowledge regarding the long-term effects of ionizing radiations in man (1, 3, 5, 6, 12).

Because of the studies of survival among radiologists then being conducted at the Johns Hopkins University School of Hygiene and Public Health by Raymond Seltser and Philip Sartwell (9, 10), the NAS-NRC initiated the Registry project as part of the existing Johns Hopkins activity, thus creating a new, more comprehensive Registry project which was to be supervised by a standing committee of the NAS-NRC. In 1960, development of the Registry at the Johns Hopkins University began as a pilot venture with modest expenditures of personnel and funds. Plans for the long-term cooperation of the participating colleges of medical specialists and their membership were worked out, and procedures for data collection, processing, maintenance, and analysis were developed. Registers were established at the participating colleges and a central statistical unit was set up at Johns Hopkins. Financial support came from the Public Health Service and the Atomic Energy Commission.[2]

In July 1968, the Registry project and responsibility for its operation were transferred to the Bureau of Radiological Health of the Public Health Service, where a Central Registry Unit is maintained. The Radiation Registry of Physicians now operates jointly with the American College of Radiology (ACR), the College of American Pathologists (CAP), and the NAS-NRC. The original plans for the Registry envisioned the involvement of at least two other specialty societies, the American College of Physicians and the American Academy of Ophthalmology and Otolaryngology. Subsequent discussions led to the decision to initiate the project with the ACR and CAP, with the idea that other societies might be invited to participate if experience showed this to be desirable. It was felt that broader participation would be easier to secure if it were demonstrated that the two "pilot" registers could be operated successfully.

It is important to clarify at this point what is meant by the terms *register* and *registry* in this report. The term *register* is defined as a listing of persons or the accumulated body of recorded data regarding those persons, whereas a *registry* is defined as the organization and process involved in the support, maintenance, and operation of a register. A single radiation registry, therefore, represents an organization which can support several registers. This is more than mere semantics. Even though the ideal research design calls for the collection of data in an identical fashion for both "cases" and "controls" in a study, the development of a registry program calls for a certain amount of improvisation. Thus the two colleges participating in the Registry program are each operating separate registers, which must be evaluated separately.

---

[1] From the Division of Biological Effects (C. S., Deputy Director), Bureau of Radiological Health, Public Health Service, Rockville, Md., and the School of Hygiene and Public Health (R. S., Associate Dean and Professor of Epidemiology), Johns Hopkins University, Baltimore, Md. Accepted for publication in January 1971.

[2] Public Health Service, National Institutes of Health Contract PH 43-64-44 and Atomic Energy Commission Contract AT(49-7)-1906 were received 1960–1965. Since 1966, The Public Health Service (Division, then National Center, now Bureau of Radiological Health) has funded the project under Contracts PH 86-66-170, CPE-R-70-0002, and CPE-R-70-0003.

The Radiation Registry was clearly defined at its inception as an attempt to establish a long-term follow-up of radiologists and comparison groups "designed to disclose such effects on life expectancy, morbidity and related characteristics as may be the result of exposure to radiation." The interest of the Registry program covers the entire gamut of biological effects of ionizing radiations. It may be said that one of its aims is the collection of data on the variables of today which may serve as indicators of the radiation effects of tomorrow.

METHODS

The basic source document of the Radiation Registry of Physicians is an eight-page, self-administered questionnaire which is mailed to members of the two colleges and returned to the respective college offices. The questionnaire has been designed to furnish information about such personal characteristics of the Registry group as age, sex, marital status, place of birth, and information regarding professional career; gross descriptions of possible exposures to ionizing radiations, including type of x-ray work, years of occupational exposures of various types, and personal exposures to diagnostic and therapeutic radiation procedures; personal exposures to other health hazards, including tuberculosis and cigarette smoke; reproductive histories which might facilitate evaluation of possible genetic effects of radiation exposure (including a history of miscarriages, stillbirths, congenital anomalies, maternal x-ray exposures, or other conditions during pregnancy); and a family history, including a survival record of parents, siblings, spouse, children, and grandchildren (including both family and respondent histories of specific conditions thought to be related to radiation exposure, such as leukemia, skin cancer, etc.).

The questionnaires remain the property of each of the respective colleges. However, they are forwarded to the Central Registry Unit in the Bureau of Radiological Health for processing and coding after they have been checked by the college offices. Elaborate precautions have been taken to safeguard the confidential nature of the completed questionnaires. All members of both colleges have been assigned Registry Code numbers which constitute the only identifying mark on the questionnaire. The responsibility for assigning the Registry Code number rests with the Central Registry Unit, and numbers are now assigned to all new members each year on the basis of cards forwarded from the college offices. The individual respondent does not sign his name, and numerous procedures have been developed to prevent individuals who need access to the questionnaires from also obtaining access to the code book which identifies the individual.

Each questionnaire, with its related documents, is kept in an individual file identified by a study number. No names are ever attached or related to the completed questionnaire. Each college, as well as the project officer in the Central Registry Unit, has a single master log of the study number assigned to an individual. The colleges maintain alphabetical files and the central unit keeps a numerical log. The Central Registry Unit also maintains current files of names and addresses of all members of the two college registers.

After the questionnaires have been forwarded to the Central Registry Unit, the information is coded and punched on IBM cards for storage and use in analysis. The identifying data on each respondent are immediately coded and punched so that current lists of respondents and nonrespondents are always available. A detailed coding system has been developed to generate a minimum of 11 IBM cards from each questionnaire. The coding system is based on experience derived during the first few years of the study, when detailed studies were conducted on a 10% sample of questionnaires as they were received by the Statistical Unit at Johns Hopkins. Repeat mailings of questionnaires are made to nonresponding members, and several other methods have been used or are being contemplated by the colleges to improve the response rate.

RESULTS

The data generated by the Radiation

Registry are classified as cross-sectional, retrospective, and prospective or longitudinal. Examples of these three types of data are given below.

I. Cross-Sectional Data

A. Composition of the Total Radiation Registry Population: The total population included in the Radiation Registry comprises all U. S. physicians who were members of the American College of Radiology (ACR) and the College of American Pathologists (CAP) in December 1961 (later changed to Jan. 1, 1962) and all those who subsequently became members of the participating colleges. By March 1970, the Radiation Registry included 7,090 members and former members of the American College of Radiology and 5,678 members and former members of the College of American Pathologists. It is an important aspect of the Registry operation that once individuals have been enrolled into the Registry, future follow-up will be attempted regardless of whether they retain their college membership or not. This has not posed a problem as yet, but it will involve extra work in tracking down individuals who drop out of a college for any reason. However, this does not represent a major problem when dealing with physicians, since they are followed continuously by the American Medical Association through its directory department.

Of the ACR members, 4,741 represent individuals enrolled in the original Registry program in December 1961; 3,115 of the CAP members were in the original group. The additional 2,349 ACR and 2,563 CAP registrants represent new members. Most of the material analyzed thus far has dealt exclusively with the original registrants.

B. Response of the Original Registry Group: When the questionnaires were returned by the original group of respondents, two peaks were notable: one covering the initial six-month period of mailing and follow-up requests and a second peak which reflects the intensive clean-up campaigns carried out first by the ACR and then, one year later, by the CAP. Somewhat different techniques were used by the two colleges, for a number of reasons. The most effective results were obtained by the American College of Radiology, which employed its local councillors in a combined telegraph and telephone campaign and achieved an overall response rate of 89.2%, compared to 77% for the CAP. The ACR response rates were at the same high level in all geographic regions of the U. S.; there was more variation by region in the CAP response rates, but these differences are not remarkable.

C. Response of New Members: The Registry is a dynamic instrument which needs continued follow-up efforts to maintain satisfactory response rates. The new members taken into the ACR in 1962 attained response rates similar to the overall response of the original group, but considerably fewer of those who were enrolled in 1963 responded. The same is essentially true for new CAP members, whose 62% response is similar to that of the original group one year previously.

D. Age Distribution of Respondents and Nonrespondents: TABLE I shows the importance of age as a variable in response to this program. There is a rather consistent inverse relationship between the age of the members and the level of response, which is to be expected. In view of the fact that future initial questionnaires will be filled out by relatively younger men, the prognosis for continuing improvement of the level of response in this program seems excellent.

Comparison of responses in the current Registry project with the response levels attained by a previous study carried out by Macht and Lawrence in 1951 (4), in which the follow-up activities were limited to one follow-up letter, reveals that the response rates have been consistently higher for respondents of all ages despite the longer questionnaire used in our study. Many radiologists did not respond to the 1951 survey but have responded to the current project either spontaneously or as the result of the persistent follow-up efforts of the college officials. There is an important difference in the orientation of these two studies, begun ten years apart. The 1951 survey was a well-conducted

TABLE I: PERSONAL DATA QUESTIONNAIRE RESPONSE ACCORDING TO AGE

Age (1961)	Yr of Birth	Radiologists (ACR) Total Sent	Radiologists (ACR) No Returned	Radiologists (ACR) % Response	Pathologists (CAP) Total Sent	Pathologists (CAP) No Returned	Pathologists (CAP) % Response
≥77	<1884	67	44	65.7	38	19	50.0
72-76	1885-89	97	79	81.4	44	27	61.4
67-71	1890-94	158	126	79.7	74	48	64.9
62-66	1895-99	211	175	82.9	135	93	68.9
57-61	1900-04	332	298	89.8	197	153	77.7
52-56	1905-09	547	498	91.0	278	212	76.3
47-51	1910-14	787	707	89.8	426	320	75.1
42-46	1915-19	869	800	92.1	525	410	78.1
37-41	1920-24	1,132	1,032	91.2	776	606	78.1
32-36	1925-29	528	487	92.2	529	435	82.2
27-31	1930-34	13	13	100.0	93	82	88.2
TOTAL		4,741	4,259	89.8	3,115	2,405	77.2

study designed to collect retrospective data on congenital abnormalities among the offspring of radiologists and comparison groups of physicians. It is unlikely that any investigator initiating a similar study today could expect to do much better in terms of the degree of cooperation elicited from groups of busy practicing physicians. Although the methodology used in the Radiation Registry initially is identical to that of the 1951 survey (*i.e.*, a self-administered questionnaire), the information generated on congenital abnormalities among offspring is really incidental to the basically longitudinal orientation which is the hallmark of an ongoing Registry program.

Information obtained regarding some of the descriptive variables of respondents is useful not only in checking the comparability of the two participating college memberships but also for the intelligent analysis of information generated by other sections of the questionnaire. These descriptive variables deal with sex (more female pathologists), marital status (more unmarried respondents in the CAP, consistent with its younger membership), birthplace (more foreign-born females than males, and more foreign-born CAP members), location of the medical school from which the respondent graduated (no marked differences between the two colleges), region of residence (no important differences), and current professional status, whether active or retired (roughly the same proportion of retired respondents in both colleges).

Another piece of cross-sectional information deals with the individual's willingness to participate in a controlled trial of dosimeters. As a result of response to this question, we now have access to a roster of 2,975 radiologists who have volunteered for studies aimed at quantitating the current level of occupational risk involved in different types of x-ray practice. This is an example of another possible by-product of the Registry program.

A major problem with which the Registry project must come to grips is the matter of "incomplete response." Even though an individual is listed as a respondent, in a number of cases only portions of the questionnaire were completed. This was rather alarming when first recognized; however, we have found that this incomplete response is seen almost exclusively in a limited number of the items dealing with retrospective data. The information of a cross-sectional nature and the type of data which will be needed for longitudinal studies have usually been answered by an overwhelming proportion of the respondents; for these items, the incomplete response levels are usually less than 5%, which seems low enough to prevent a serious bias from being introduced into future statistical analyses. Specific areas in which the incomplete responses are significant enough to cast doubt upon the usefulness of the derived data will be mentioned later.

II. Retrospective Data

The type of information most readily generated from this questionnaire survey is, quite understandably, retrospective in character. We present a few findings dealing with such information simply to illustrate some of the features of these data. Many of the more interesting items of information have not yet been processed and tabulated.

A. Factors Other Than Irradiation: The problem of the effect of initial selection factors on radiologist survival was examined. It has been suggested that physicians who are in poor health are more apt to choose a sedentary type of practice or one which is primarily hospital- or office-based rather than one which involves house calls. One reason for choosing pathologists as a comparison group was that the same factors which influence the choice of radiology as a

TABLE II · REPRODUCTIVE HISTORY: SEX OF OFFSPRING

	Radiologists (ACR)	Pathologists (CAP)
Total live births	10,905	4,306
Total offspring*	11,034	4,400
Males	5,009	1,881
Females	4,521	1,908
Not stated	1,504	611
Sex ratio (% males)	0 52	0 49

* Includes multiple births

specialty might operate in the choice of pathology as a field of specialization. We found a slight but unimpressive excess of radiologists who gave a history of having chosen their specialty as a result of illness. This seems to bear out the relative comparability of these two college memberships in regard to this factor of "initial unfavorable selection."

Preliminary analyses thus far have revealed no remarkable differences in factors which might influence the comparability of the two groups of medical specialists, such as smoking habits, prior experience with tuberculosis, or urban-rural residence.

B. Nonoccupational Radiation Exposure: There may be an important preventable occupational hazard of the field of radiology, *i.e.*, an excessive exposure to nonoccupational diagnostic x rays. The crude data show only that a greater proportion of radiologists have been subjected to medical diagnostic x-ray procedures (exclusive of routine chest films and dental x-ray examinations). If these data are valid and hold up on more refined analysis, the classical type of occupational exposures to irradiation may be found to be less important than the exposures which are "indirectly occupational" in view of the radiologists' greater accessibility to x-ray equipment. Some previously obtained preliminary data indicate that there is considerably more x-ray exposure among radiologists' families than among pathologists' families. This type of data will always be suspect in view of the possibility that radiologists may give a better history of radiation exposures, since they would remember the procedures better. This is an excellent illustration of the advantages of collecting such data for future use rather than relying on the retrospective survey.

C. Possible Effects of Irradiation: Some of the possible genetic effects of irradiation, which might be detected from the data accumulated on the responding members of the two participating colleges, were examined. One of the most interesting of these is the possible effect of paternal radiation exposure on the sex ratio of offspring. One proposed hypothesis has been that the presence of radiation-induced dominant lethal changes in the x chromosomes of the father would be expected to kill off the female offspring but not the male, resulting in an excess of male births. (Conversely, inasmuch as the male derives its only x chromosome from the mother, maternal radiation-induced damage to the x chromosomes should result in the death of the male offspring. The reverse is not necessarily true in the female offspring if the lethal gene is recessive, since the female also possesses an x chromosome from the father.)

Some preliminary sex ratio data derived from the Registry experience were compared with those of previously published studies reported by Newcombe dealing with the effects of paternal radiation exposure (7). For this purpose, all radiologists in the Registry were regarded as "exposed"; a much more refined analysis will be needed in order to separate out those offspring born prior to the father's entrance into the field of radiology. However, even taking this into account, these data represent a group of exposed fathers considerably larger than any reported previously, including the Atomic Bomb Casualty Commission group (8). The difference in proportion of male births between radiologists and pathologists is consistent with the previously stated hypothesis (TABLE II). The data have been broken down by family size, which demonstrates that the proportion of male offspring decreases among responding pathologists' families as the family size increases; this is not true for the radiologists' families. The magnitude

TABLE III. REPRODUCTIVE HISTORY: CONGENITAL ANOMALIES REPORTED

Type of Anomaly	Radiologists No.	Radiologists Rate/1,000 Pregnancies	Pathologists No	Pathologists Rate/1,000 Pregnancies
Heart and blood	56	5.1	30	6.8
Muscles and joints	40	3.7	17	3.9
Bones and cartilage	154	14.1	86	19.7
Gastrointestinal tract	31	2.8	16	3.7
Genitourinary tract	68	6.2	23	5.3
Central nervous system	21	1.9	22	5.0
Sense organs	99	9.1	45	10.3
Developmental arrest	50	4.6	21	4.8
Others	225	20.6	82	18.7
TOTAL	744	68.1	342	78.2

of the sex ratio shift is impressive for all three classes of family size (as measured roughly by the number of reported pregnancies).

In order to check this information more closely, we decided to look at the data on sex of offspring as reported in two separate parts of the questionnaire. In addition to questions dealing with reproductive history, there is also an item dealing with family history which asks for the current survival status of all children, as well as the year of birth and sex of each child. We felt that the tabulations should be roughly comparable for these two sections, although one might expect a slightly greater number of offspring reported in the section on family history. When the sex ratio data determined from these two sources were compared, the total number of liveborn offspring was indeed comparable for both sections of the questionnaires returned by the radiologists. However, there was a remarkable excess of some 2,000 pathologist offspring reported under the family history but missing from the reproductive history. The explanation for this is contained in the "unknowns," representing questionnaires in which the section on reproductive history was not completed. This was true for 32% of the responding pathologists, in contrast to 11% for the responding radiologists. The reason for this specific deficiency in the completeness of the questionnaires has not yet been determined. There is evidence that a number of men felt that they obviously did not have a "reproductive history," since they had never been pregnant! If this is the case and the section was omitted as a result of improper questionnaire design, a specific questionnaire dealing exclusively with this subject might be used to obtain the data. If, on the other hand, there is a general reluctance on the part of pathologists to furnish this type of information, the potential of the Registry program in the area of elucidating possible genetic effects of irradiation will be seriously limited. At any rate, in view of the large proportion of pathologist offspring for whom data are missing, we must be extremely cautious in interpreting the sex ratio data at this time.

The data on congenital abnormalities have not yet been completely tabulated. However, the level of completeness of response is apparently excellent in this area, with only 3.6% of the pathologists and 4.3% of the radiologists omitting the question. At present, there are 744 "congenital anomalies" of all types among the offspring of radiologists and 342 such anomalies among the offspring of pathologists (TABLE III).

Data on reported miscarriages and stillbirths show a remarkable similarity between the two groups. Information was derived from the same section on reproductive history previously used to provide sex ratio information, and it is interesting to speculate why the large group of "nonresponding" pathologists did not seem to influence these results. Possibly the factors influencing the failure to complete this section of the questionnaire may not be related to pregnancy history or sex of offspring in any way; the nonrespondents to this question might actually be a representative sample of the entire responding group. If this is the case, the sex ratio data presented above would reflect the true situation.

There are certain well-known limitations inherent in the use of a self-administered questionnaire to obtain retrospective data of this type. The memory factor becomes important in evaluating the validity of certain types of data: the older the respondent, the less likely that he or she will remember all of the details requested in the reproductive, personal, or family history. On the whole, however, there is a considerable advantage in having respondents who are all qualified specialists and completely familiar with the language. Notwithstanding the general deficiences in this method of obtaining information, an unusual body of data has been obtained with respect to the probable high level of reliability of the information on the initial questionnaire

It must be recognized that these types of data could have been collected without establishing a registry, as was done in the previously cited surveys. Therefore, the expense and time of maintaining an ongoing registry operation must be justified on grounds other than the types of information available from the retrospective or historical approach.

III. Prospective Data

The real justification for establishing a radiation registry is related to the longitudinal or prospective studies and analyses which are possible only if such a registry has been established and is maintained. It is sometimes difficult to keep this fact in mind, since the cross-sectional and retrospective data are readily available for analysis and discussion, whereas there is very little to show for the longitudinal aspect of the registry even after a number of years.

A. Factors Other than Irradiation: Data are not yet available, but in time there will be longitudinal information on the smoking practices of members of the two specialty groups.

B. Nonoccupational Radiation Exposure: Through updating the questionnaire and obtaining information on new members, there will be an opportunity to determine nonoccupational exposure as the members go through life. Special studies can be carried out to validate any marked differences that appear between the two groups. The suggestive differences observed so far will be tested.

C. Occupational Radiation Exposure: No valid data are yet available on quantitative estimates of x-ray exposures. The data to be obtained from repeat questionnaires and special dosimetric studies will offer opportunities to study trends in the use of x rays by different generations of radiologists and other physicians.

D. Possible Effects of Irradiation: The data which can be potentially generated longitudinally from the Radiation Registry should provide information on both somatic and genetic late effects of ionizing radiations.

Survival is the most straightforward and perhaps most valid information which can be derived from the Registry. Since basic age data are available on all college members regardless of whether they return the questionnaire or not, it will be possible to derive age-specific death rates for the members of these two specialties as the years progress.

A later study by Seltser and Sartwell (11) indicated that the type of occupational exposures to radiations used by radiologists prior to 1940 had an effect on survival. That study was based entirely upon reconstruction of membership rosters of various specialty societies and follow-up for survival status of all individuals who had ever been members of those societies. It was not possible to investigate other factors which might have influenced survival, such as smoking habits or pre-existing illnesses which might have selectively biased the composition of the specialty groups being studied.

Estimates based on current mortality rates of radiologists indicate that of the 4,200 original respondents from the American College of Radiology register, 1,450 would be expected to die within the next twenty years. Of these deaths, 250 would occur during the next five years, with an additional 300 deaths during the subsequent five years, 400 deaths during the third five-year interval, and another 500 deaths during the fourth five-year period. If the mortality analysis for this sizable group could be correlated with information recorded in the Radiation Registry files, there would be an opportunity to draw inferences with considerably greater confidence than was possible when such information was not available. As a result of the procedures developed during the radiologist mortality study at Johns Hopkins, there is an excellent mechanism available for review of all deaths of American physicians. At present, all American Medical Association death records are sent from Chicago for review and radiologist and pathologist deaths can be detected. This will be especially helpful in determining

Table IV: Cause of Death

Classification	ICD No.*	Radiologists Respondent (%)	Radiologists Non-respondent (%)	Radiologists Total (%)	Pathologists Respondent (%)	Pathologists Non-respondent (%)	Pathologists Total (%)
All causes		236(100.0)	74(100.0)	310(100.0)	90(100.0)	68(100.0)	158(100.0)
Heart	401.1-443	109(46.2)	25(33.7)	134(43.2)	49(54.4)	27(39.7)	76(48.1)
Cancer	147-203	46(19.5)	11(14.8)	57(18.4)	14(15.6)	8(11.8)	22(13.9)
Leukemia	204.0-204.4	2(0.8)	2(2.7)	4(1.3)	1(1.1)	3(4.4)	4(2.5)
Vascular lesions of the central nervous system	330-334	19(8.1)	6(8.1)	25(8.1)	6(6.7)	7(10.3)	13(8.2)
Accidents	816.0-836.0	7(3.0)	6(8.1)	13(4.2)	6(6.7)	2(2.9)	8(5.1)
Chronic nephritis	592	2(0.8)	...	2(0.6)			
Pneumonia	490-493	5(2.1)	3(4.0)	8(2.6)		2(2.9)	2(1.3)
Diabetes	260	1(0.4)	...	1(0.3)		1(1.5)	1(0.6)
General arteriosclerosis	450	2(0.8)	1(1.4)	3(1.0)	1(1.1)	1(1.5)	2(1.3)
Cirrhosis of the liver	581.0-581.1	1(0.4)	...	1(0.3)	...	1(1.5)	1(0.6)
Suicide	970.2-978	5(2.1)	1(1.4)	6(1.9)	3(3.3)	2(2.9)	5(3.2)
Hyperplasia of the prostate	610	...	1(1.4)	1(0.3)	...		
Hernia and intestinal obstruction	561.0-561.5 and 570.0-570.5	3(1.3)	...	3(1.0)	1(1.1)	...	1(0.6)
Diseases of the circulatory system	465-466	3(1.3)	1(1.4)	4(1.3)	...	1(1.5)	1(0.6)
All other causes		26(11.1)	12(16.2)	38(12.3)	8(8.9)	7(10.3)	15(4.5)
Unknown	795.5	5(2.1)	5(6.8)	10(3.2)	1(1.1)	6(8.8)	7(4.5)
Total admissions		4,295(100.0)	482(100.0)	4,741(100.0)	2,405(100.0)	710(100.0)	3,115(100.0)
Total deaths		236(5.5)	74(15.4)	310(6.5)	90(3.7)	68(9.6)	158(5.1)

* ICD (International Classification of Diseases, World Health Organization)

TABLE V: CANCER DEATHS REPORTED JAN. 1962-APR. 1968

Classification	ICD No.	Total No. of Cancer Deaths	Radiologists			Pathologists		
			Respondents	Nonrespondents	Total	Respondents	Nonrespondents	Total
All neoplasms		87	48	13	61	15	11	26
Digestive	150-159	26	11	4	15	7	4	11
Respiratory	160 0-165	14	10	2	12	1	1	2
Male genital organs	177-179 9	11	9	1	10		1	1
Urinary	180-181 8	7	5	1	6	.	1	1
Skin	190 0-191 9	3	1	.	1	2	..	2
Brain and central nervous system	192-193 9	3	1	1	2	..	1	1
Other	140 0-148 194-199	8	4	1	5	3	...	3
Lymphoma	200 0-203	7	5	1	6	1	...	1
Leukemia	204 0-204 4	8	2	2	4	1	3	4

survival status of nonrespondents. The participating colleges are also a source of reports of deaths, since survival status is reviewed annually for all active dues-paying members. As of April 1968, there had been 468 deaths among the original Registry members; the specific causes of death are shown in TABLE IV.

It may be estimated that of the expected deaths from *cancer and leukemia* occurring among the 4,200 responding radiologists, 200 may be due to cancer, of which 15–20 may be due to leukemia. Investigation of these cases could be carried out using the case-control method of study, since it would be possible to employ both matched pathologists and other radiologists for comparison purposes. The cancer deaths by type among the original groups of radiologists and pathologists as of April 1968 are given in Table V.

In addition, recent studies indicate a suggestion of an across-the-board effect on mortality from most major causes of death. Cause-specific data therefore may be most important for determining possible effects of irradiation on other major diseases as well.

In regard to *genetic effects*, it is anticipated that the data on sex ratio and congenital abnormalities among offspring of radiologists and pathologists will be more valid on a longitudinal study basis than on a retrospective basis. Many new members of both colleges represent young families still in their child-bearing years. Data collected on these groups should accumulate rapidly during the coming years. It should also be possible to investigate second-generation effects of radiation exposures by conducting special studies of the fertility patterns of the offspring and looking for congenital malformations among the grandchildren. More than 1,670 grandchildren have been reported by ACR members and 690 by CAP members. Forty-six congenital anomalies have been reported thus far in ACR grandchildren (2.8%) and 23 in CAP grandchildren (3.3%).

SUMMARY

This is the first report of the Radiation Registry of Physicians, conceived and gradually established during the past decade. The Registry was developed as a vehicle for the long-term follow-up of radiologists and comparable medical specialists for the purpose of studying biological effects of prolonged exposure to ionizing radiations. The study population is comprised of the total living membership of The American College of Radiology and the College of American Pathologists as of December 1961 and thereafter. The basic source of information is a detailed, self-administered questionnaire handled confidentially by the two colleges; the processing of data is done separately in a central registry unit of the Public Health Service.

To date, the principal types of tabulated data available are cross-sectional and retrospective; longitudinal data, except for some survival figures, have not yet been generated. The future production of longitudinal data is the primary goal of the Registry. Important as cross-sectional and historical data are, they can be gathered by survey techniques without the need for registries. The collection of longitudinal data on an ongoing basis offers the advantage of reliability of current data as compared with recollected data, as well as the opportunity for soundly based prospective studies.

Because the Registry includes total population groups, it can serve as a frame for sampling subgroups of radiologists or pathologists for intensive study. Sampling on a known probability basis, even if it involves only small numbers, provides the basis for the use of conventional statistical tests and evaluation.

There are already many suggestive leads from the data concerning the nonoccupational use of irradiation by radiologists and their families, the diminished occupational exposure of younger radiologists, and possible alterations in the sex ratio of offspring. The Registry is not designed to yield quantitative dosimetric information, but this weakness could be overcome by studying samples of practices and exposures and relating these to the study of population exposure to x rays in the United States which was carried out in 1964 (2) and repeated in part in 1970.

The feasibility of developing a physician registry which may prove useful in delineating biological effects of occupational exposure to ionizing radiations has been demonstrated. The existence of the Registry poses a challenge to those responsible for establishing safety standards in the radiation field. A number of studies might employ appropriately drawn samples of physicians for intensive studies of dosimetry and related areas. Such studies would have the advantage of yielding a maximum amount of information economically. However, the Registry's major contribution is the opportunity for longitudinal follow-up of responding physicians and the compilation of increasingly relevant and useful data over the years with adequate opportunities for the validation of such data.

Acknowledgments: We wish to acknowledge the invaluable assistance of Miss Jeannette Westlake, Research Associate, Department of Chronic Diseases, who was research supervisor for the project at Johns Hopkins from 1964 to 1968, and Mrs Edythalena A. Tompkins, Epidemiologic Studies Branch, who was project director at the Bureau of Radiological Health from 1968 though 1970.

Division of Biological Effects
Bureau of Radiological Health
Public Health Service
12720 Twinbrook Parkway
Rockville, Md 20852

REFERENCES

1. Court Brown WM, Doll R: Expectation of life and mortality from cancer among British radiologists. Brit Med J 2:181-187, 26 Jul 1958

2. Gitlin JN, Lawrence PS: Population exposure to x-rays, U S, 1964. Public Health Service Public. No. 1519 Washington, D.C., Govern Print Off, 1964

3. Lewis EB: Leukemia and ionizing radiation. Science 125:965-972, 17 May 1957

4. Macht SH, Lawrence PS: National survey of congenital malformations resulting from exposure to roentgen radiation. Amer J Roentgen 73:442-466, Mar 1955

5 March HC: Leukemia in radiologists. Radiology 43:275-278, Sep 1944

6. March HC: Leukemia in radiologists in a 20 year period. Amer J Med Sci 220:282-286, Sep 1950

7. Newcombe HB: Genetic effects in populations, with special reference to studies in man, including ABCC results. Radiat Res 16:531-545, Apr 1962

8. Schull WJ, Neel JV: Radiation and the sex ratio in man. Science 128:343-348, 15 Aug 1958

9 Seltser R, Sartwell PE: Ionizing radiation and longevity of physicians. JAMA 166:585-587, 8 Feb 1958

10. Seltser R, Sartwell PE: The application of cohort analysis to the study of ionizing radiation and longevity in physicians. Amer J Public Health 49: 1610-1620, Dec 1959

11. Seltser R, Sartwell PE: The influence of occupational exposure to radiation on the mortality of American radiologists and other medical specialists. Amer J Epidem 81:2-22, Jan 1965

12. Ulrich H: The incidence of leukemia in radiologists. New Eng J Med 234:45-46, 10 Jan 1946

13 Warren S: Longevity and causes of death from irradiation in physicians. JAMA 162:464-468, 29 Sep 1956

Mr. CARTER. Until recently—I think it has been generally an accepted fact, Dr. Kennedy, that radiologists had a higher incidence of cancer and leukemia than other groups. But since they have been using protective measures in the past few years, this higher rate is no longer evident.

I think that is correct; is that not right?

Mr. VILLFORTH. Let me just summarize what we have submitted for the record, if I may.

Mr. CARTER. Yes, sir.

Mr. VILLFORTH. The results of the previous study indicate—and I will quote from a portion of the report which we have already submitted for the record which was sent out in 1961—

> A descriptive overview of the first questionnaire was published in 1971, and although it furnished several suggested leads, the data at that time were not adequate to draw firm conclusions. The data from the second questionnaire

which I am saying we are in the process of analyzing—

> has been compiled, and several papers are being developed. The first of these show that radiologists and their families have a higher frequency of personal medical diagnostic and therapeutic radiological procedures than do pathologists and their families.

Mr. CARTER. That is true, what you said.

Mr. VILLFORTH. We have to wait for the remainder to be completed.

Dr. KENNEDY. It is a pretty interesting finding, Dr. Carter. Among other things, it says some things about the faith you can have in control populations as opposed to experimental ones.

Mr. CARTER. I disagree with you. If a study shows just that fact, then certainly we want to know how much money has been put into the project and any other conclusions that have been reached.

What specific steps do you follow after notifying a manufacturer of his noncompliance?

Mr. VILLFORTH. Of noncompliance?

Mr. CARTER. Yes.

Mr. VILLFORTH. Depending on the nature of the noncompliance, if it is a case in which the manufacturer of the product, something related to the assembly line of the product is involved, we would disapprove their introduction of the machine into commerce. We would disapprove the testing program. The manufacturer must submit his testing program to us.

Now if there is something wrong at the manufacturing point, we would disapprove that testing programs, which means the manufacturer could not then introduce any products into commerce until the problem was resolved. Initially, we can stop the introduction into commerce and then sit down and find out exactly what the nature of the problem is and whether, if some products have previously been introduced into commerce, they must be recalled and how this can be done.

Maybe the product can be repaired on site; maybe it would have to be recalled.

Mr. CARTER. What is the status of your agency's regulatory authority regarding certification and inspection of medical devices used in radiological health care?

Mr. VILLFORTH. With regared to Medical Device Amendments, we are working with our sister, Bureau of Medical Devices, to utilize the provisions of the Medical Device Amendments as they relate to radiological products. Some of these products, as you know, most of these products are in a classification system right now. We have utilized the provisions of their act for compliance actions or recall actions when appropriate on products which fall outside the direct scope of electronic products.

Example: The X-ray film processor is not, by definition, an electronic product under the Radiation Control for Health and Safety Act of 1968. But the Medical Device Amendments allow us, when we find that there is a problem with that processor, to have it brought into compliance. So this authority allows us to handle all elements of radiological systems, those which are electronic products and those which are not.

Mr. CARTER. One final question. What do you think of the use of film badges that radiologists or technicians wear to indicate the amount of exposure to radiation? Do you think they are effective?

Mr. VILLFORTH. The personnel monitoring system, whether it is a film badge or the type of chips Dr. Kennedy talked about before, regardless, the personnel monitoring device is an extremely effective tool to allow the individual, first of all, to determine if some of their practices need improvement. It is an excellent tool to determined if they become a little careless.

It is also an extremely important tool to understand if the exposures are such that the individual has to worry about radiation consequences. But like any device, it measures the radiation, records the radiation with some limitations to a very small area. These thermoluminescent dosimetry chops are just a few millimeters in cross section and will only record the radiation that strikes them.

It is an extremely effective tool for improving the quality of radiological practice.

Mr. CARTER. Does this type of badge ever measure refracted X-rays?

Mr. VILLFORTH. Those X-rays which are scattered which might be scattered of the wall or all shielding could certainly be——

Mr. CARTER. Thank you very kindly. We are in agreement.

Mr. ROGERS. Mr. Maguire.

Mr. MAGUIRE. Thank you, Mr. Chairman.

Dr. Kennedy, we are all aware of the fact that X-rays are standard in a number of places in our society where medical examination are called for. I am thinking of chest X-rays as a part of an employee physical examination, for example, whether that is for a job in a government agency or the private sector. I am thinking about hospital admissions where, regardless of what the malady may appear to be, chest X-rays are sometimes taken as a standard part of the admission process.

I am wondering what you think about that. In view of your testimony, is the general use of X-rays without some indication of a specific problem or without the presence of some special category of person subjected to some particular stress or hazard—a coal miner, for example—advisable? Should we have such general screening use of X-rays?

Dr. KENNEDY. I think that trajectory of informed medical opinion has been to increasingly discourage routine procedures of that kind. The medical radiation guidance proposal signed by the President earlier this year discourages routine chest X-rays. That will soon be implemented for our department by an interagency group under our lead.

I think that that is the advice generally being given with regard to routine dental X-rays. It doesn't mean dental X-rays aren't valuable under particular indications of need, but a routine, by rote or by requirement or by habit, application of that requirement is, I think, almost everyone now agrees, a bad idea.

Mr. MAGUIRE. I have been looking through the testimony that we are going to receive shortly from the American College of Radiology. Perhaps this is taking things a bit out of order, but they indicated, talking about hospital admission chest X-rays, that such X-rays serve two purposes: to identify health problems which might affect the patient's care while he is in the hospital; for example, whether there might be any special difficulties administering anesthesia or anesthetic; and second, to protect other patients from contagious disease, where you might have tuberculosis.

Do you have any further comment on that particular rationale?

Dr. KENNEDY. Mr. Maguire, I have not read their testimony and I think my view of it would depend on whether that was described as an absolutely routine procedure. It seems to me where there is no indication that infectious disease were likely to be a problem and no earlier criteria for eligibility used routine examination history and so forth, I think they would probably agree that the application of a rote procedure requiring them would be inappropriate.

I would guess they would, but I haven't read their testimony, and it really isn't appropriate for me to put words in their mouths.

Mr. MAGUIRE. As I understand it, the present legislative authority which came into existence in 1968 does not permit you to order correction of safety defects in X-ray equipment or to enforce against manufacturers any standards for equipment manufactured prior to 1968; is that correct?

Dr. KENNEDY. Yes, that's correct.

Mr. MAGUIRE. Do you think that is a problem?

Dr. KENNEDY. Well, it might be, but it is a little difficult to tell how much of a problem it is. We are still able to reach through State cooperative programs, through programs like BENT and DENT, to find out about overexposures that are associated with such instruments; not all of them, but a pretty high frequency.

Furthermore, we believe that the proportion of those machines in use is declining fairly rapidly and that the proportion of radiographs taken by them is declining as more facilities are using the newer, post-certification equipment.

It would, I think, be a large and not terribly profitable effort for us to undertake to bring all of those into compliance, even having the authority to do so.

Mr. MAGUIRE. What is the life of a piece of X-ray equipment?

Dr. KENNEDY. My colleague says 20 years.

Mr. MAGUIRE. So we are half-way along with something that was manufactured and put into service in, say, 1968?

Dr. KENNEDY. That's right.

Mr. MAGUIRE. The law also provides no authority to seize defective or dangerous or noncompliance equipment; is that correct?

Dr. KENNEDY. Yes.

Mr. MAGUIRE. Suppose on that little card you showed us earlier you get some results back which are very discomforting and you make a request and nothing happens; what then?

Dr. KENNEDY. These are cooperative programs with the States, and the normal thing then will be a visit from a State inspector. I think it is our understanding—and John can correct me if I am wrong—in general, the States report a very high level of compliance with their invitations to improve the performance of those machines.

In short, I am not aware, Mr. Maguire, that we are encountering problems with recalcitrant folks out there who are not trying to improve their equipment when we tell them there is a problem.

Mr. MAGUIRE. That's encouraging.

Mr. VILLFORTH. Mr. Maguire, may I amplify?

Mr. MAGUIRE. Yes.

Mr. VILLFORTH. I think when you consider the inventory of X-ray machines that are out there to date, about 270,000 machines, and the fact that our colleagues in the 50 State agencies inspect probably in the neighborhood of 50,000 X-ray machines a year, that in the course of the time since 1968, many of these machines have been looked at and some of them many times. And we have not received an indication that some of those older machines, prior to 1968, are really in such bad shape as a result of some improper manufacture or some defective component such that there is a real public health problem. I think if there were a problem, it would have been identified by the fact that at least each one of those make and model machines has certainly been inspected at least once.

Mr. MAGUIRE. I thought we were dealing with an aggregate problem here which was composed of a lot of discreet individual cases where the exposures were somewhat greater than they should have been or there was a double exposure which was a result of a circuit malfunction.

Shouldn't there be some authority to seize equipment where it might be necessary? Of course, one would hope that it would not be, but if it might be necessary, why not have that authority?

Mr. VILLFORTH. Yes. The point that I would make——

Mr. MAGUIRE. Yes; you should have that authority.

Mr. VILLFORTH. If it were a problem, I think maybe one needs to look at that possibility of authority.

The point I would make is those machines have been looked at by the States—those older machines—and, to the extent that that kind of a problem which you describe would have been identified, I think that we could—and I am not aware of that for the older machines—but I think we could have gotten that problem solved.

Mr. MAGUIRE. Suppose it takes some extra money. It is not just a question of making an adjustment, let's say, in the machinery. Suppose it is going to be costly to make the machine expose people 20 percent less; what happens then?

Mr. VILLFORTH. If the machine is routinely doing something wrong as a result of its manufacture, as the illustration you gave, which turns out to be unacceptable and one cannot get the cooperation of the manufacturer of the industry to correct that, now that is a voluntary process, because we are talking about machines prior to 1968, and if one cannot elicit the cooperation of the user, the hospital or the private practitioner to correct that, and if one cannot get the State agency to bring some influence on the user to stop having a machine that is overexposing the public, then we have a problem that might fall under the seizure provisions of the Food and Drug Administration as a separate portion of the Radiation Control for Health and Safety Act.

I cannot illustrate for you how serious that kind of problem is. I am not aware of the extent of that problem for those older machines in 1968.

Mr. MAGUIRE. It is at least something we should look at.

Mr. VILLFORTH. Yes, sir.

Mr. MAGUIRE. What about new products? You don't have, as I understand it, any premarketing review of new products. Is that correct? Or the ability to set performance standards for them. Is that correct?

Mr. VILLFORTH. We have the ability to set performance standards for any new electronic product; yes, sir.

Mr. MAGUIRE. How do you do that if you don't have any premarket review?

Mr. VILLFORTH. I am not sure that a premarket review would be necessary in all situations.

Mr. MAGUIRE. How on earth do you set standards for something if you don't know what it is?

Mr. VILLFORTH. If you are saying——

Mr. MAGUIRE. If you don't know what people are producing or about to sell on the market?

Mr. VILLFORTH. We have requirements for notification of certain products which would allow the manufacturers to report to us; not premarket approval, but notification of these products. And that would allow us the opportunity to ask more questions.

Now we do not have premarket approval under the Radiation Control for Health and Safety Act. Again, I think the Medical Device Amendments would be applicable here.

Dr. KENNEDY. Mr. Maguire, this may be helpful or it may not. I think the more usual case will be a new product that is a variant of an existing product. CAT scanners would be an example of this. We are amending the standard to accommodate them.

It is hard to think of a machine so novel that it would be something entirely different and require, rather than an amendment, the identification of a new technology and the establishment of a new authority.

Mr. MAGUIRE. Do you have any standards, now, for example, for CAT scanners?

Mr. VILLFORTH. Amendments to the existing X-ray standard are being developed.

Mr. MAGUIRE. The CAT scanners have been out scanning for the last 3 or 4 years.

Mr. VILLFORTH. The basic X-ray performance standard is applicable to computed tomography units. There are certain aspects of computed tomography, however, which are different and, therefore, we want to sharpen up, if you will, our X-ray performance standard for computed tomography units, and there is an amendment being developed now to allow that.

But the basics of the X-ray performance standards are applicable to computed tomography. So the unit is under a degree of surveillance.

Dr. KENNEDY. Excuse me.

Mr. MAGUIRE. I only have a couple more minutes.

What about guidelines for the safe use of this equipment? What is the current authority there and should you have anything that you don't have? This really must be my last question.

Dr. KENNEDY. We have no explicit authority to set guidelines for safe use. We are undertaking all of our instructional and educational and guideline distributing programs, assuming we have that authority implicitly.

Mr. MAGUIRE. Did you want to add something else on the other question?

Dr. KENNEDY. No.

Mr. MAGUIRE. Thank you.

Mr. ROGERS. May I interrupt at this point?

There is a second call to the floor for a vote. The committee will stand in recess for 10 minutes.

[Brief recess.]

Mr. ROGERS. The subcommittee will come to order, please.

May we have order?

Thank you.

Mr. Commissioner, what is the scope of the problem as you see it now as far as X-ray machines, dental machines and its effect on the public from excess exposure to radiation?

Dr. KENNEDY. Well, Mr. Chairman, I would say that in broad strokes, it is a problem that has to be met largely, I think, by changing the behavior of consumers and providers. I think that there is more room in the system for reducing that portion of our citizens' exposure than there is in compliance activities carried out by the Food and Drug Administration under our rules.

Mr. ROGERS. Do you concur with the 30-percent figure that you think that is a justified figure of overexposure to the public?

Dr. KENNEDY. I am not sure it is exactly right, Mr. Chairman, but I think it is in the ball park. I think most studies of particular procedures that are done more carefully come up with 20 to 40 percent or 15 to 40 percent reduction potentials, so I don't think 30 percent is an unreasonable figure, though I wouldn't be surprised to see it adjusted either upward or downward as we gain more experience.

Mr. ROGERS. What about pregnant women now; do we know the amount of procedures still being carried on? Do you have any estimate?

Dr. KENNEDY. I think our estimates show that certain procedures that expose the abdominal area have been sharply reduced.

Mr. ROGERS. I understand. But what is the magnitude of the problem still there? Do we have any idea of the extent of the problem still existing?

Dr. KENNEDY. Let me ask my colleague for some help on that.

John, do we know anything about how many exposures are done per year?

Mr. VILLFORTH. I cannot recall. I know with various estimates of the amount of pelvimetries done in the United States. In light of the discussions yesterday by Dr. Phillips, it certainly appears, whatever that number is, it is unreasonably high in light of his investigation and that the number of those exams can almost be reduced to zero.

I think he said he only found two such exams in 71 months at the hospital where he had put the controls and procedures into effect. So whatever the number is, it appears the number of pelvimetry exams could be sharply reduced.

Mr. ROGERS. Somebody, I think, estimated about 6.9 percent of all pregnant women were still receiving that procedure.

Mr. VILLFORTH. The number we have is that of the 3,000,500 U.S. live births in 1970, 850,000, or 23 percent of these women were X-rayed.

Mr. ROGERS. Twenty-three percent X-rayed?

Mr. VILLFORTH. Twenty-three percent in 1970.

Mr. ROGERS. So that would mean that much of that is excess?

Mr. VILLFORTH. In light of what Dr. Phillips said yesterday, certainly much of that would be unnecessary. I am not sure what the figure might be in 1978; we would have to look at that.

Mr. CARTER. I believe he said about the only indication for it was a breech presentation.

Mr. VILLFORTH. Yes sir; I believe he said vaginal delivery for breech presentation.

Mr. CARTER. He said a breech presentation. It can be delivered either way; vaginally or by cesarean section.

Mr. ROGERS. Do we have an up-to-date figure? If he said 6.9 percent, that would amount to about how many? And it is your figure you have 23 percent?

Mr. VILLFORTH. I want to correct that figure; the 23 percent includes all X-rays to pregnant women, not just pelvimetries. I think your question relates to pelvimetry.

Mr. ROGERS. Pelvimetry is what I wanted to know. I understand it was 6.9 percent; almost 7. So that would be how many women are being exposed to that, which probably is not a correct procedure?

Mr. VILLFORTH. 200,000.

Mr. ROGERS. Over 200,000?

Mr. VILLFORTH. Yes.

Mr. ROGERS. What about screening; is it necessary to have chest X-rays for screening, for instance, before you are hired; to go through an exam and have your chest X-rayed? Is that a proper procedure, you feel, at this time?

Dr. KENNEDY. I think most of the recommendations are that as a routine procedure, it be discontinued. That doesn't mean chest X-rays wouldn't be important, given some indications from history or others, but I think the prevailing opinion now, and certainly the medical radiation guidance promulgated earlier this year recommends discontinuation of that practice as a routine procedure.

Mr. ROGERS. It is my understanding—and you might check this for us and ask them to comment for the record on this—that the

Commissioned Corps of the U.S. Public Health Service requires X-ray exams before hiring. I don't presume you would know offhand if that is true or not.

Mr. **VILLFORTH.** As a member of the Commissioned Corps, it is generally true, yes, sir.

[The following information was received for the record:]

PHS COMMISSIONED CORPS POLICY ON PREEMPLOYMENT CHEST X-RAY EXAMINATIONS

Mr. Rogers' statement in the record to the effect that the PHS Commissioned Corps "requires X-ray exams before hiring" is correct. Calls to duty each year entail approximately 1,800 physicals that include a chest X-ray examination (Commissioned Personnel Manual, Part 2, Subchapter CC29.3, Personnel Instruction 5—copy enclosed). Commissioned Officers may also receive a chest X-ray at time of their routine physical examinations, every two years up to age 40, and every year after age 40 (Personnel Instructions). Although the chest X-ray examination is optional, officers customarily receive it. Approximately 2,185 active duty officers receive a physical each year (on-duty and those leaving the Service) out of the total complement of approximately 7,000 active duty officers in the Corps.

We are in the process of investigating the efficacy of entry physical X-ray exams as well as X-rays for periodic physicals. We are trying to ascertain how the yield of occult and treatable cardiopulmonary disease compares with the cost and radiation risk of the examination. The results of our studies will be applied not only to Federal policies but will be disseminated to the private sector as well.

Mr. **ROGERS.** Have you had any communications with them about that?

Dr. **KENNEDY.** We certainly will, Mr. Chairman, because it is for the Public Health Service and for Public Health Service institutions that we have been given a lead in implementing the radiation guidance recently promulgated. So I would say we have an appropriate target there.

Mr. **ROGERS.** I also understand that a chest X-ray is part of the National Institutes of Health physical exam.

Dr. **KENNEDY.** You mean beyond those NIH employees who also happen to be members of the Commissioned Corps?

Mr. **ROGERS.** Yes.

Dr. **KENNEDY.** I don't know about that, Mr. Chairman.

Mr. **ROGERS.** Does anybody here know?

Could you check that?

[The following information was received for the record:]

NIH POLICY ON EMPLOYEE X-RAY EXAMINATIONS [1]

1. Preemployment Chest X-Ray Examinations

(*a*) Exams for all civil service employees are provided on a voluntary basis, except for patient care and wage-grade employees. These employees are required to undergo an X-ray exam.

(*b*) A chest X-ray is required for all employees when diagnostically indicated. Indications include either existing disease (obtained via medical history) or a positive tuberculin skin test.

(*c*) Approximately less than 20 percent of all NIH employees undergoing physical exams receive a chest X-ray.

2. Occupational Health Examinations

(*a*) Chest X-ray exams are provided according to the following criteria:

- Persons aged 18-30 years—every 5 years
- Persons aged 31-44 years—every 2 years
- Persons aged 45 yrs. or older—every year

These exams can be waived by the employee. Non-waivable annual chest exams are required for firemen, glass blowers, or persons with past asbestos exposure.

---

[1] Information obtained from Dr. Brandt, Occupational Health Service, NIH.

(*b*) No occupational low back exams are performed.

Mr. VILLFORTH. I am under the impression an X-ray is part of the physical examination, if offered, and the individual has the right to refuse it.

Mr. ROGERS. I understand they have a right, but there are not too many who do.

Mr. VILLFORTH. This is not generally understood. As Dr. Kennedy said, we have some work to do with this authority that has been given to the Food and Drug Administration to bring the PHS components in line with the President's directive. That will be taking place.

Mr. ROGERS. I would hope you would give us a report on your contacts with other departments of government advising them about this and what reaction you get from them. I think that would be helpful for the committee to have this knowledge.

[The following information was received for the record:]

IMPACT OF PRESIDENTIAL DIRECTIVE ON MEDICAL RADIATION GUIDANCE

The Presidential Directive, which contained recommendations for Federal facilities, can be expected to have some impact on the private sector's use of medical radiation. Since the guidance was only issued several months ago, the full impact on the private sector has probably not been reached. Some of that impact can be expected to be positive and some negative.

Positive Impact:

Since the Directive contained useful advice concerning the use of medical radiation, it is likely that health professionals who are concerned about radiation protection will utilize this information as indices of ways to improve their practice. Thus, the guidance can be expected to have an educational and motivational impact. To a lesser extent, educated and concerned citizens (not health professionals) might also become better informed concerning good radiological health care practices by reading the Presidential Directive. The Bureau of Radiological Health has attempted to foster both of these impacts by:

a. Publishing on February 13, 1978, a BRH Bulletin article, which was disseminated to the thousands of people on the Bureau mailing list (both professionals and lay persons), describing the main features of the Presidential Directive and its development, and offering to supply further information to interested persons. We have received, to date, 19 responses to this bulletin article asking for additional information; and,

b. Preparing an "open letter" (with a copy of the Presidential Directive attached) to persons on the Bureau's mailing list, urging them to read the Presidential recommendations carefully and to study ways in which the recommendations can be adapted to suit the circumstances in private sector radiological health care facilities. This letter is expected to be completed and ready for wide dissemination shortly. This latter approach, that of adapting the Presidential recommendations to suit the circumstances which occur in private sector radiological health care utilization, is a direct result of the direction from the Assistant Secretary for Health in his April 28th memorandum to heads of the Public Health Service components, asking them to consider ways in which the recommendations in the Presidential Directive can also be incorporated into their health care programs, in order to improve the radiological health care of citizens, in general, even though they may not be treated at Federal health care facilities.

Another positive impact has been the increasing awareness shown by other Federal agencies (such as the State Department) concerning the problem of indiscriminate use of x radiation prescribed under various Federal programs which affect the radiation exposure of people in the private sector. The Bureau is working with EPA in order to coordinate directions to all Federal agencies regarding this problem.

Negative Impact:

Because the Presidential Directive contains recommendations which were written to address problems known to occur in Federal facilities, as opposed to private sector medical facilities, there have been some misunderstandings. For example, both the Bureau and EPA have received inquiries from members of the chiropractic profession complaining that recommendation 1 in the Directive is an unfair and possible illegal means of preventing chiropractors from operating x-ray equipment, because recommendation 1 does not mention them as a profession that can order x rays. Both the Bureau and EPA have responded to these inquiries, but there is probably no doubt that the inquiries themselves represent only the tip of an iceberg. Additionally, because the recommendations themselves are relatively short and not discussed in any detail, there is considerable opportunity for misunderstanding of the intent, scope, and methodology for implementation of the recommendations. It is necessary that additional advice be given to the private sector, analogous to the advice which the Interagency Working Group will be giving to the various Federal agencies in order to clarify and aid their implementation of the Presidential recommendations. The Bureau of Radiological Health will be responding to this need both in its forthcoming task proposals for planning for the upcoming year, as well as in its several medical radiation recommendation projects which are presently under development. An additional negative impact is the fact that some State agencies may take the Presidential recommendations and make them regulatory. For example, the State of Vermont has attempted to do this with recommendation 10 which deals with maximum x-ray examination exposure values or Entrance Skin Exposure Guides (ESEG). There are a variety of important reasons why it is inappropriate to take these recommendations and make them mandatory, but the most important reason is that that obviates the principle of medical professional judgment which must be allowed to override, in order to take into account unexpected individual circumstances which cannot be anticipated by some overall recommendation or general rule of action.

FEDERAL IMPLEMENTATION OF THE PRESIDENTIAL DIRECTIVE REGARDING MEDICAL RADIATION GUIDANCE

With respect to the implementation of the Presidential Directive in the Federal government, we have already met with several agencies under a variety of circumstances. First, the Bureau of Radiological Health is a member of the Interagency Working Group, a panel of Federal agencies chaired by the Environmental Protection Agency under their FRC authority. This group originally devised the recommendations in the Presidential Directive, and is now actively pursuing the question of better implementation throughout the Federal government. The Bureau of Radiological Health is chairing a subcommittee of that working group, entitled the Subcommittee on Implementation and Coordination. It is the function of this subcommittee to discuss necessary followup clarifications and revisions to the Presidential recommendations as specified in the document, as well as to track problems of the various agencies in meeting its provisions.

Additionally, the Bureau of Radiological Health is acting under the directive of the Assistant Secretary for Health to coordinate the implementation of the Presidential Directive within the Public Health Service agencies which conduct medical care activities, such as the Public Health Service and the Indian Health Service hospitals and clinics. In anticipation of the Assistant Secretary's Directive, the Bureau of Radological Health has met informally with representatives of the Public Health Service facilities, the Indian Health Service facilities, and the National Institutes of Health. Discussions have been conducted on the implementation of the Directive, including interpretation of the twelve recommendations and a preliminary assessment of the responsibilities which the Directive entails for these agencies. The Commissioner of the Food and Drug Administration has communicated with each of the Public Health Service agencies and the Health Care Financing Administration, requesting their nomination of an individual who can represent the agency in detailed discussions concerning the implementation of the Directive. A Conference is being scheduled for the month of September at which time these agency designees will discuss the Directive with the Bureau, and the process of implementing the Directive will formally begin. The first major step will be the acquisition of certain important information, such as the number, type, and location of all of the x-ray equipment under the control of each agency, with technical information regarding the radiological health inspection of the equipment. Based upon an analysis of that information, the Bureau will be able to assist each agency in establishing a plan, including necessary budget and manpower requirements, to fully comply with the Presidential Directive.

Mr. **Carter**. Mr. Chairman, if you would yield on that. I would like to know what your military physicians, naval physicians, and air force physicians are doing in this regard. Are they following your guidelines for use of X-ray?

Dr. **Kennedy**. Dr. Carter, I can't answer that question. The guidelines have only recently been promulgated, and we have just been assigned by the Surgeon General of the Public Health Service the task of leading the effort of implementing them. We will be back to you with a response as soon as we find out.

[Testimony resumes on p. 332.]

[The following information was received for the record:]

SUMMARY OF CURRENT CHEST X-RAY PRACTICES AND POLICIES AMONG FEDERAL HOSPITALS/AGENCIES

On January 26, 1978 the President of the United States approved twelve recommendations entitled, "Radiation Protection Guidance to Federal Agencies for Diagnostic X Rays" (Federal Register, Vol. 43, No. 2, Pages 4377-80, February 1, 1978). These recommendations provide guidance on the ordering and conduct of medical and dental x-ray examinations in Federal health care facilities. Two of the recommendations address ordering of x rays including chest screening. Specifically, the Directive recommends that "routine or screening examinations in which no prior clinical evaluation of the patient is made, should not be performed unless exception has been made for specified groups of people on the basis of a careful consideration of the magnitude and medical benefit of the diagnostic yield, radiation risk, and economic and social factors."

In an effort to initiate follow-up and implementation of these Presidential recommendations, it was necessary to determine the existing policies for ordering x rays within the various departments and agencies in the Federal Government. Therefore, telephone inquiry was made to the appropriate office, generally the health unit or personnel office, within each organization to determine its individual x-ray ordering policy.

The policies for ordering x rays were found to vary within the various departments and agencies contacted. Generally, about 50 percent of the policies call for occupational health examinations, including a chest exam for employees over 40 years of age, every two years. In about another 25 percent of the agencies contacted the chest x-ray examination is normally performed, but may be waived by the employee if he or she so desires. In certain other agencies, where employees may be subject to slightly increased risk, personnel may be required to undergo chest x rays at annual or two year intervals (e.g., FBI agents, Drug Enforcement Administration agents, foreign service employees, mining inspectors, etc.). It was also determined that the Civil Service Commission does not require individuals to undergo a routine chest x-ray examination upon entry into Federal service, although employees are required to complete a medical history questionnaire. The USPHS Commissioned Corps requires a chest x ray before Corps appointment and subsequent x rays every two years until age 40 and annually thereafter.

A summary of the information received from Federal agency and department personnel is attached. The information presented in the summary table is based upon discussions and opinions derived from the various agency personnel rather than quoted from agency regulations. An attempt was made to obtain the specific regulations governing the requirements for x-ray examinations; however, in most cases, regulations were not furnished.

SUMMARY OF DIAGNOSTIC EXAMS AMONG CABINET DEPARTMENTS

Department	No X Rays Obtained on Employee	Chest X Ray Preemployment Exams Required	Routine Health Exams (X Rays Required)	Chest X Ray Waivable At Discretion of Employee	Executive Level Chest X Rays at Discretion of Employee
AGRICULTURE	X				
HUD			Over 40 yrs every 2 yrs		
COMMERCE	X				
JUSTICE					
Law Enforcement Assistance Adm.				All employees	
Bureau of Prisons		X		All employees	
Immigration & Naturalization Services					Available to GS-14
FBI		X	To 34 yrs every 3 yrs; annually thereafter		
Drug Enforcement Administration		X	Annually regardless of age		
Marshal Service		X	To 39 yrs every 2 yrs; annually thereafter		
LABOR				Employees over 40 yrs every 2 yrs	

SUMMARY OF DIAGNOSTIC EXAMS AMONG CABINET DEPARTMENTS

Department	No X Rays Obtained on Employee	Chest X Ray Preemployment Exams Required	Routine Health Exams (X Rays Required)	Chest X Ray Waivable At Discretion of Employee	Executive Level Chest X Rays at Discretion of Employee
TRANSPORTATION				Employees over 40 yrs every 2 yrs	GS-14 approximately every 14 months
STATE		X	All foreign service employees over 18 every 2 yrs (CXR & panorex dental film) Less than 18yr receive skin test; CXR if positive.		GS-15 annually
INTERIOR			Over 40 yrs annually		
Bureau Mines & Enforcement			All mining inspectors every 2 yrs.		
Law Enforcement Bureau			All agents every 2 yrs.		
ENERGY				Employees over 40 yrs every 2 yrs	
TREASURY			Some employees every 2 yrs Employee age criteria is determined by each agency		
ENVIRONMENTAL PROTECTION AGENCY				Over 40 at GS-11 and GS-12 annually	Any age GS-13 and above annually

SUMMARY OF DIAGNOSTIC EXAMS AMONG CABINET DEPARTMENTS

Department	No X Rays Obtained on Employee	Chest X Ray Preemployment Exams Required	Routine Health Exams (X Rays Required)	Chest X Ray Waivable At Discretion of Employee	Executive Level Chest X Rays at Discretion of Employee
NATIONAL REGULATORY COMMISSION		X		Employees over 40 yrs every 2 yrs	
DEPT. OF HEALTH, EDUCATION & WELFARE					
Public Health Serv.					
Div. of Federal Employees Health, Health Services Administration			Over 40 yrs every 2 yrs		
Indian Health Service	X				
Div. of Personnel Management, FDA				Employees over are 40 every 2 yrs Every 5 yrs under age 40	
USPHS Com. Corps		X	To age 40 every 2 yrs 40 and over annually		
Center for Disease Control				Civil service - over 40 every 2yrs COs & dependents - every 2 yrs.	

SUMMARY OF DIAGNOSTIC EXAMS AMONG CABINET DEPARTMENTS

Department	No X Rays Obtained on Employee	Chest X Ray Preemployment Exams Required	Routine Health Exams (X Rays Required)	Chest X Ray Waivable At Discretion of Employee	Executive Level Chest X Rays at Discretion of Employee
PHS Continued					
Natl. Heart & Lung Institute	X				
Natl. Cancer Institute	X				
Social Security Administration			Under age 39 every 3 yrs. Age 40-49 every 2 yrs. over age 50 annually (This requirement may not be enforced)		
DEPT. OF NAVY					
Bethesda Naval Hospital			Under 36 yrs every 3 yrs 36 and over annually		
Bureau Medicine and Surgery			Annual if high risk employment		
Naval Shipyard, Long Beach		X	Periodically since fibrogenic dusts are present		
DEPT OF AIR FORCE		X	Every 4 yrs		
Wilford Hall Hospital, San Antonio, TX	Not required on admission but usually taken				

SUMMARY OF DIAGNOSTIC EXAMS AMONG CABINET DEPARTMENTS

Department	No X Rays Obtained on Employee	Chest X Ray Preemployment Exams Required	Routine Health Exams (X Rays Required)	Chest X Ray Waivable At Discretion of Employee	Executive Level Chest X Rays at Discretion of Employee
DEPT. OF ARMY		X			
VETERANS ADMIN.	X				
POSTAL SERVICE	X				
WHITE HOUSE	X				

Mr. CARTER. I have a response already.

Dr. KENNEDY. You have one?

Mr. CARTER. I have the response. They certainly are not carrying it out. One of my colleagues who came back from the Capitol told me he had a PA and lateral chest X-ray and an abdominal X-ray thrown in to boot, although he had protested mildly about having it.

This is occurring to our own physician here in the Capitol; and he is a nice man.

Dr. KENNEDY. We will try to look into that promptly, Dr. Carter.

Mr. ROGERS. And if you would and report to the committee. That, I think, you can do right away; getting to the Federal Government immediately.

I presume you are also contacting the necessary colleges and the professions and their organizations. Is that in the process of being done, Mr. Commissioner?

Dr. KENNEDY. Yes, it is, Mr. Chairman. We have just received and just responded to that instruction from the Surgeon General. So I am talking about things that are just starting to happen, but it is starting and we will be reporting to your subcommittee.

Mr. ROGERS. That is for Federal facilities. I am talking beyond Federal, like the AMA, various colleges of specialties.

Dr. KENNEDY. Yes, I understand. Our instructions explicitly ask us to examine ways in which the implementation that we execute for those institutions over which we have direct authority can be extended to the private sector, to those institutions over which we do not have control. So we will be doing that.

Mr. ROGERS. Would you let us know your time schedule and what response you get?

[The following information was received for the record:]

EFFORTS TO EXTEND THE PRESIDENT'S MEDICAL RADIATION RECOMMENDATIONS TO THE PRIVATE SECTOR

Within the next month, we anticipate sending out an "open letter" (with a copy of the Presidential Directive attached) to professional organizations, health professionals, and private citizens interested in radiological health on the extensive Bureau of Radiological Health mailing list. This open letter will urge interested people to read the Presidential recommendations carefully and to study ways in which the recommendations can be adapted to suit the circumstances in private sector radiological health care facilities. We will also be discussing this principle of adapting the Presidential Directive for the private sector with the Public Health Service agencies so that all the Public Health Service programs which impact on the health care in this country can appropriately incorporate the intrinsic radiation protection philosophy contained in the Presidential Directive. The specific plans for this approach have not yet been formulated. The process of formulating those plans will begin at the September conference of the PHS agency representatives.

Mr. ROGERES. What have you done or what are you doing about the fact 6.9 percent of pregnant women are still being exposed?

Dr. KENNEDY. Mr. Chairman, our educational programs on that are aimed very specifically at that population. We think that this is the only way to get this problem dealt with effectively. We have had very good cooperation from ACOG.

Mr. ROGERS. What is ACOG?

Dr. KENNEDY. The American College of Obstetricians and Gynecologists. Our efforts have been to warn women about radiation; and to have them to raise the possibility of their pregnancy with their doctors and also to ask an examining physician to be conscious of that problem. The difficulty is, the result of these efforts are difficult to measure quickly.

Mr. ROGERS. What has the college done as a result of your contact?

Mr. VILLFORTH. May I amplify on what we have, Mr. Chairman?

Mr. ROGERS. Certainly.

Mr. VILLFORTH. The concern that we have overordering criteria, which is that type of approach that was presented to you yesterday by Dr. Phillips, has been put into a program that we have at the University of California, headed up by Dr. Reynold Brown. We have asked Dr. Brown to put together panels, and specifically three panels, to look at certain areas and see if the type of ordering criteria that Dr. Phillips discussed and presented can be put into effect.

One has to do with skulls; one has to do with routine chest X-rays that you were talking about. The other has to do with pelvimetry.

We asked Dr. Phillips to be a part of this panel so the results and successes he had can be shared with us. Once that is done, and the panel agrees on certain criteria as to what it should be used for and should not be used for, then we hope to have that criteria tested before that can be put into a broader program.

Perhaps the ultimate utilization of this process is through the health care financing mechanism, if the profession can agree on these criteria.

Mr. ROGERS. Have the gynecology and obstetric doctors disagreed?

Mr. VILLFORTH. In terms of what we are doing in the pelvimetry area. I don't think so.

Mr. ROGERS. What have they done? Have they sent out notice of warnings or notice of change, do you know?

Mr. VILLFORTH. I am not aware what they done in regards to reducing it based on what Dr. Phillips presented yesterday.

Mr. ROGERS. I don't know if they have done anything on what he has done yesterday. I wonder if we had made a request that they advise their members of this danger to exposing pregnant women.

Mr. VILLFORTH. In general, the American College of Obstetricians and Gynecologists is concerned about this issue.

Mr. ROGERS. I know they are concerned, and I know you can't speak for them. Perhaps this line of questioning is unfair. Do you know whether or not they have taken any positive steps?

I get a nodding in the back. If you have knowledge, let me know. Could you identify yourself and let us know?

Ms. VAN BRUNT.[1] I am Deborah Van Brunt. I am in consumer education for the Bureau of Radiological Health.

ACOG has already promoted that poster, for example, in their newletter and informally with their local affiliates.

Likewise, agreements have been made for the American College of Radiology, and the American Hospital Association to distribute those kinds of materials plus medical recommendations to hospitals and clinics with radiology facilities.

---

[1] Ms. Van Brunt was in the audience and responded to Chairman Rogers questions.

Mr. ROGERS. What about the College of General Practitioners, GP's?

Ms. VAN BRUNT. I think we are talking about the American College of Obstetricians and Gynecologists.

Mr. ROGERS. I am talking about the general practitioners now.

Ms. VAN BRUNT. The family physicians?

Mr. ROGERS. Family physicians too.

Ms. VAN BRUNT. We have not yet made those contacts.

Mr. ROGERS. Because many of them handle the patients.

Ms. VAN BRUNT. We are in the process of systematically approaching all types of health professional organizations.

Mr. ROGERS. Will you let us have your time schedule? I will ask staff to check with those colleges to see what warnings they have sent out, how they have handled it with their membership.

[Testimony resumes on p. 400.]

[The following materials were received for the record:]

SUMMARY OF FDA ACTIVITIES
TO REDUCE UNNECESSARY MEDICAL RADIATION EXPOSURE
OF THE HUMAN EMBRYO AND FETUS

FDA activities to reduce radiation exposure to the human embryo and fetus can be divided into four categories: (1) development of voluntary medical recommendations; (2) consultation in the development of non-FDA policy statements; (3) development and promotion of professional education programs; and, (4) development and promotion of consumer/patient education materials.

DEVELOPMENT OF VOLUNTARY MEDICAL RECOMMENDATIONS

Program efforts to develop medical recommendations on x rays in pregnancy began with the submission of a contract report in August 1974 entitled, "A Concept and Proposal Concerning the Radiation Exposure of Women." The document was reviewed within the Bureau of Radiological Health as well as by the Bureau's Medical Radiation Advisory Committee (MRAC). In December 1975, a Notice of Intent was published in the FEDERAL REGISTER. The Notice presented nine questions designed to elicit information relating to development of a voluntary recommendation. Approximately eighty responses were received and analyzed. Based upon that analysis, a report entitled "Clinical Methods of Avoiding Medical X-Ray Exposure of the Human Embryo and Fetus: A Technical Overview" (attached) was prepared and distributed to over 800 interested individuals. The report analyzed the benefits and limitations of existing guides and presented an alternative approach for minimizing embryonic and fetal exposure. Comments received on that approach have been factored into a proposed recommendation which will be published shortly in the FEDERAL REGISTER. Following an analysis of comments on the proposed recommendation, final recommendations will be promulgated.

Proposed FDA recommendations to minimize x-ray exposure of the human embryo and fetus have been discussed several times during development with the National Council on Radiation Protection and Measurements, the American College of Radiology, the American College of Obstetricians and Gynecologists, and the BRH Medical Radiation Advisory Committee. These discussions served to insure broad consultation with those groups acknowledged to possess professional expertise in areas pertinent to this concern. Recommendations thus developed can be expected to be inherently more credible as a result of this unanimity.

The proposed and final recommendations are expected to be published in the FEDERAL REGISTER during FY 79, with ample opportunity for comment by the medical community. Implementation of the recommendations will be achieved through cooperative educational channels, such as publication in professional medical journals and consumer publications, and development and dissemination of pamphlets and posters.

CONSULTATION

FDA has consulted with and reviewed policy statements on medical radiation exposure of women developed by the American College of Radiology (ACR), the American College of Obstetricians and Gynecologists (ACOG), and the National Council of Radiation Protection and Measurements (NCRP). This activity has resulted in the promulgation of policy statements consistent with the proposed FDA medical recommendation.

PROFESSIONAL EDUCATION EFFORTS

Professional education activities have focused in three areas to date.

1. The Efficacy of Pelvimetry:

In September 1975, FDA published a review of the efficacy of the pelvimetry x-ray examination. The study analyzed 67,078 single deliveries of 1,000 gms or greater in 16 hospitals, yielding 4,599 pelvimetry examinations. The study concluded that: (1) there appeared to be no uniform set of indications for performing pelvimetry; (2) a normal pelvimetry gives the physician little confidence that a Caesarean section will not be necessary; and, (3) the duration of labor is not significantly altered by pelvimetry in those women needing a Caesarean section for cephalopelvic disproportion. This report was published in a national medical journal and presented at a national medical society meeting.

In FY 78, the pelvimetry examination was selected as one of several examinations in an overall plan to develop criteria for the judicious ordering of diagnostic x-ray examinations. A panel of physicians to develop the criteria was also selected and a meeting of the panel is tentatively scheduled for September. This panel will include several authors of pelvimetry efficacy studies, including Drs. Phillips, Kelly, and Campbell. Each agrees with us that the following testing and implementation strategy is appropriate.

FY 79 plans include further panel meetings, and submission of a final report on high-yield criteria for pelvimetry. During FY 80 and the first half of FY 81, plans include testing the criteria in controlled clinical trials, using both PSRO and non-PSRO facilities. FY 81 implementation plans include publishing the criteria, issuance to third-party carriers and PSRO's, integration into professional education packages, and distribution of patient education materials. The last quarters of FY 80 and FY 81 also will include evaluaton of the use of pelvimetry criteria by using the PSRO's to obtain exam frequency data. Although this timetable extends over several years, we believe that clinical testing of the criteria is crucial in order to avert possible patient injury or death which could result from inappropriate or erroneous criteria.

2. Reaching Practicing Physicians:

In a second activity, a program was pilot tested at Massachusetts General Hospital to: (1) increase physician awareness of the need to determine pregnancy prior to requesting an x-ray examination; and, (2) encourage physicians to consider the use of modified x-ray examinations on pregnant or possibly pregnant women. Results of the study have been considered in FDA's proposed recommendation.

3. Reaching Medical Students:

A third ongoing activity in the professional education area is the integration of specific message units on x rays in pregnancy into the Radiological Health Sciences Learning Laboratory, FDA's learning system for medical students and radiology residents, that is now in use in over 70 percent of U.S. medical schools. Included is information related to the efficacy of the pelvimetry examination and the FDA, ACR, ACOG, and NCRP guides. As further information is developed it will be incorporated into appropriate sections.

CONSUMER EDUCATION

Several materials have been developed to inform consumers of their role in reducing x rays during pregnancy. To increase patient awareness, two versions of a poster - one, a wall hanging and the other, a desk size version - have been developed with joint sponsorship of the Bureau of Radiological Health and ACOG asking women to tell their physicians if they are or believe they might be pregnant. A Spanish version will be available soon. Copies of the poster are being distributed through cooperative efforts with outside groups.

During 1977, a 60-second public service announcement was aired on behalf of FDA with the same message.

A May 1977 article in FDA Consumer entitled "X Rays and Pregnancy" explained the possible hazards of x rays during pregnancy and presented precautions the patient could invoke.

Currently being reproduced is a 14-minute slide/tape show, "X Rays: So You Want To Be In Pictures?". It describes consumer involvement in the diagnostic x-ray process and reviews patient precautionary measures such as informing the physician of a certain or possible pregnancy.

An FDA pamphlet "We Want You To Know About X Rays During Pregnancy" is expected to be available in the near future. The pamphlet was developed in cooperation with the American College of Obstetricians and Gynecologists and the American College of Radiology. The pamphlet, which will complement the poster developed earlier, is designed for use in waiting rooms and for physicians to give to individual patients.

Finally, a mini-lesson for high school students is currently under development. (Mini-lessons are self-contained teaching packets for health or science teachers.)

CLINICAL METHODS OF AVOIDING MEDICAL X-RAY EXPOSURE OF THE HUMAN EMBRYO AND FETUS: A TECHNICAL OVERVIEW

I. INTRODUCTION

X radiation and other types of ionizing radiations have been shown to be effective in producing a wide variety of developmental defects in the mammalian embryo and fetus, including that of humans. Although the available evidence is not universally accepted, especially for effects reported to occur in animals and humans from doses below about 50 rads, it is nevertheless sufficiently convincing to warrant some caution when human embryos and fetuses are exposed to radiation. Of all sources of ionizing radiation, medical radiation contributes the greatest amount of man-made radiation to the U.S. population (26). Although much of medical radiation is indisputably necessary for proper health care, a part alleged by some to be as high as 30% may be unnecessary (26). Consequently, medical radiation has received much attention by scientists and clinicians concerned about radiogenic risks to the developing embryo and fetus.

Various recommendations have been suggested and implemented which are intended to decrease the possibility of irradiating the abdomen of pregnant women during the first month or so of gestation, when the pregnancy is most likely to be unsuspected. (No clinical recommendations, other than general admonitions about radiation hazards to the unborn child, have been proposed which relate specifically to reducing the radiation exposure of the fetus at other times during gestation). Recently, however, the scientific basis of these recommendations has been questioned (6), stimulating an active re-examination of the whole issue. It is the purpose of this Technical Overview to summarize their advantages and limitations, and to suggest consideration of an alternative approach which not only emphasizes the necessity for referring physicians to first determine whether or not their patients might be pregnant and to factor that information into the decision concerning the x-ray request, but also stresses the need for reducing x-ray exposure of fetuses throughout gestation.

II. BIOLOGICAL RISKS TO THE EMBRYO FROM IONIZING RADIATION

A. Introduction

The biological basis for this document will be thoroughly covered in another staff document (11) currently in preparation. For this reason, only a very brief summary will be presented in this report.

Experimental studies with animals and some limited human epidemiological studies and case reports have indicated that x-ray exposure represents a hazard to the unborn child. The magnitude and kinds of possible effects depend upon the amounts and types of ionizing radiation received and the stage of fetal development when exposure occurs.

The first trimester of human pregnancy, especially the first 2 weeks after conception, carries the highest risk of abortion induced by radiation. Other somatic effects have been reported as well. The second through sixth weeks following conception are probably the most critical with respect to production of observable anomalies in the unborn child (4, 29, 32, 41). Radiation exposure of the fetus during all stages of pregnancy has been associated with an increased incidence of leukemia and other childhood cancers (2,10,22,42,43). There is some suggestion that the carcinogenic effect appears to be greatest for exposure during the first trimester (2). During the second and third trimesters, fetal irradiation is associated with growth and developmental malformations manifested by physiological and behavioral changes, some of which may not become apparent until later in life (4,16,37).

Since both the maternal and fetal gonads may be exposed, abdominal irradiation during any stage of pregnancy may also produce genetic effects in two individuals (at least!). Furthermore, abdominal irradiation of a prospective mother prior to conception may result in genetic changes which could be transmitted to her offspring; for example, some controversial evidence has suggested an increased risk of mongolism and cancer in children born to mothers receiving x rays before conception (5,13,25,42,45,46).

Consequently, examination of the literature supports the conclusion that at no time during gestation can the developing embryo or fetus be irradiated without incurring risk of some biological effect. Each stage of pregnancy has associated with it the risk of certain radiation induced effects; the kind of effect and its probability of occurence varies with the age of the embryo or fetus and the absorbed dose. It may be true that the greatest magnitude of effect from a given dose occurs as a result of exposure early in pregnancy, but it does not follow from this that no effects occur as a result of exposure late in pregnancy, as is frequently implied.

In order that the biological consequences of ionizing radiation to the developing embryo and fetus can be fully appreciated in proper context, it is necessary to discuss not only the types of effects but also their occurrence as a function of dose. The magnitude of potential radiological risks to the embryo and fetus have been examined in this report. However, estimates of risk, although a useful quantification of data, contain uncertainties because: by their nature, human epidemiological studies usually contain unavoidable complexities; extrapolation of available data from animal studies to humans is tenuous; and there are few reported risk estimates in humans for effects other than cancer. For example, reliable estimates of the incidence in humans of congenital malformations or subtle somatic and genetic effects are unavailable. Nevertheless, some estimates of the magnitudes of radiological risks to embryos and fetuses, based upon presently available data, limited though it may be, is potentially useful for clinicians.

Using x-ray examination rates from a 1963 national survey, Boice and Burnett (3) estimated that in 1970, 805,000 pregnant women in in the United States (23 percent of those who were pregnant that year) received x-ray examinations of all types (Table 1). They further estimated, that during the first trimester, nearly 22,000 of these women received abdominal x-ray examinations (each woman receiving on the average 1.2 exams). If it is assumed that these examinations were divided equally throughout the first trimester, then it follows that approximately 7,000 fetuses would have been exposed in the first month of pregnancy, the period when it is most difficult to detect a pregnancy. (This latter estimate only represents live births and does not include pregnancies terminated because of spontaneous or induced prenatal death. Furthermore, it should be noted that the use of 1963 examination rates may not be a good indication of current practice; however, these are the only national rates available.)

Table 1. Estimated Numbers of Fetuses Irradiated During Abdominal X-ray Examinations

	Percentage	Number
U.S. 1970 live births	---	3,500,000
Pregnant women x rayed	23	805,000 (3)
Fetuses irradiated during abdominal x-ray examinations:		
All trimesters	37 (a)	298,000
First trimester	7.5 (b)	22,000
Second trimester	4.9 (b)	15,000
Third trimester	87.6 (b)	261,000

(a) Corresponds to the total number of abdominal x-ray examinations performed as a percentage of x rayed pregnant women (i.e., (0.37)(805,000) = 298,000).

(b) Correspond to the number of abdominal examinations performed in the first, second and third trimesters respectively as a percentage of all pregnant women receiving abdominal x-ray examinations (e.g. (.075)(298,000) = 22,000).

It is interesting to note that the estimated number of fetuses irradiated during the third trimester is more than seven times the estimated number irradiated earlier in pregnancy.

B. Risk of Teratogenic Effects

The possible teratogenic effects of x-ray exposure in utero can be considered in three categories: (1) gross morphological changes, varying from polydactyly and subtle spinal abnormalities to exencephaly and severe skeletal malformations; (2) severe mental retardation, often with accompanying microcephaly and smaller-than-normal stature; and (3) more subtle functional changes in the central nervous system, including alterations in neurological function or behavior.

With the exception of a few individual case studies in humans, almost all of the available evidence for gross morphological effects as a result of prenatal irradiation is derived from animal experiments, in which it has been demonstrated that the the dose range most likely to produce these effects is on the order of 25-400 rads, delivered in the early stages of organogenesis (21,29,31-35,40,41,48). It is not yet possible to make a definitive statement as to the probability of doses below 25 rads inducing structural anomalies. In considering the results of available animal studies, the BEIR Committee has stated, "These effects become less and less likely as the dose descends below 100 rads." (26) The consensus appears to be that although there may be no threshold for the cellular effects produced by intrauterine irradiation, an "effective" threshold may exist for the clinically observable results of this cellular damage. In other words, it may be that a minimum number of critical cells must be damaged or killed in order for observable structural defects to occur.

Adding to the uncertainty is the usual problem in applying animal data to humans; although certain fundamental qualitative similarities are presumed to exist in the response of human and rodent embryos to radiation, the extrapolation of quantitative results from animals to humans is subject to considerable error. To make matters worse, there is the serious problem of dosimetry. Many of the animal studies use exposure at the skin to measure the amount of radiation received by the subject. Given the large differences in body dimensions between rodents and humans, and the correspondingly large differences in radiation attenuation in tissue, interpreting this animal data for humans becomes all the more subject to error.

It is thus very difficult to draw any firm conclusions from this animal data with respect to the risk of gross congenital malformations in humans as a result of x-ray exposure during pregnancy, except to say that these effects appear extremely unlikely unless the dose received by the embryo were to exceed 25 rads, a level considerably above that generally encountered in diagnostic radiology. This situation contrasts markedly with the known risks from certain other teratogens. For example, the probability of congenital anomalies as a result of rubella during the first month of pregnancy is roughly 50% (15) and the tranquilizers meprobamate and chlordiazepoxide, when administered during the first 6 weeks of gestation, have been estimated to more than quadruple the normal incidence of some anomalies (23).

With respect to gross mental retardation as a result of intrauterine irradiation, the bulk of available information derives from the Japanese atomic bomb survivors. Here, estimated doses above 50 rads were associated with an increased risk of mental retardation, accompanied in many instances by microcephaly and a general diminution in stature.

The Japanese data leaves largely unanswered the question of more subtle, functional changes in the central nervous system as a result of prenatal irradiation, in that the design of the studies necessitated that the investigators screen the exposed children only for "profound" retardation, that is, that they limit their investigations to children who were grossly retarded (26). Thus, there may have been effects on intelligence and behavior less severe than that which could have been detected by these studies. These effects may have occurred at doses considerably lower than 50 rads, a possibility which can neither be corroborated nor discounted at the present time.

Along the same lines, animal experiments have shown damage to nerve cells at 10 rads (26). Although this did not result in a measurable deficit in function, considering the large differences between the intellectual capacity of rodents and humans and the difficulties in measuring subtle functional effects on the human central nervous system, it is certainly possible...although not provable at present...that doses on the order of 10 rads or less to the human embryo can produce small alterations in intelligence or behavior. Thus in the light of available human and animal studies, the possibility of functional central nervous system effects must be borne in mind when considering the potential consequences of x-ray examinations during pregnancy.

C. Cancer Risk: First Month of Pregnancy

In the United States, the estimated annual incidence of all cancers in children under 15 years of age is 12.5/100,000 (24). A recent publication by Bithell and Stewart (2) has updated and reviewed the risk from the Oxford Survey of

Childhood Cancers and has extended the follow-up to include children up to 15 years of age. This study suggests that irradiation during the first trimester appears to carry a higher risk of childhood cancer compared with irradiation in the second or third trimesters, although the number of irradiated children in the study was too small to draw a firm conclusion. For irradiation during the first month, the authors have estimated a lower limit of risk for all cancers of 2.5 relative to unity in non-irradiated children. This estimate was based upon radiographic examinations with a mean of 4.6 films per case. Assuming an average annual incidence rate of childhood cancer of 12.5/100,000 and a risk factor of 2.5, for each group of 7,000 pregnant women receiving abdominal x rays during the first month of pregnancy, we estimate the occurrence in the U.S. population of approximately one additional case of childhood cancer accumulating each year for the 15 years after birth (see Table 2). If each year for 15 years or more, a population of 7,000 women is given abdominal x-ray examinations during their first month of pregnancy, an estimated total of 15 cases of cancer in children under 15 years of age would occur annually.

It is important to note that there are other critical underlying assumptions to this estimate. For example, the estimate assumes that fetal x-ray doses per film and the number of films per examination are comparable between the British experience several years ago and United States practice in 1970. Obviously if the resultant fetal doses per examination should be different, the risks estimated for the United States would be expected to differ. Unpublished analysis by the Bureau of Radiological Health of average exposures per abdominal film in the United States (1970) has revealed that resultant average fetal doses may have been two times lower than in the British experience. Counterbalancing this is the fact that the relative risk factor of 2.5 estimated from the Oxford Survey is a lower limit and may in fact be several times greater. (At this writing, more precise evaluation of the first month risk was not possible). If the relative risk

Table 2. Derivation of Estimated Annual Incidence of Childhood Cancers Resulting from Abdominal X-ray Examinations of Pregnant Women During the First Month of Pregnancy

	Annual Rates	Annual No. in U.S.
Fetuses Irradiated 1st Month		7,000
Childhood Cancer Cases:		
Natural Incidence	12.5/100,000	0.9
Exposed to X Rays	31.4/100,000 (a)	2.2
Additional (excess) cases resulting from x rays	18.9/100,000	1.3

(a) This rate corresponds to the naturally occurring rate (12.5/100,000) times the increased risk factor (2.51) assuming that the exposed women were given abdominal examinations averaging 4 to 5 films each, with fetal doses comparable to those in the Oxford Survey.

estimate in the Oxford Survey for the first trimester (8.95) were used, the estimated number of cancers would be increased. Consequently, the estimate for the United States should be understood to have a large error factor associated with it.

D. Cancer Risk: All of Pregnancy

Fetal irradiation during the remainder of pregnancy has also been associated with an increased risk of childhood cancers. In the Oxford Survey, abdominal examinations averaging 2 to 3 films each at any time during pregnancy were estimated to increase cancer risk by 50% during the first 15 years of the child's life (2).

An estimated 298,000 unborn children may be exposed annually to abdominal x rays throughout all of pregnancy (Table 1). Assuming, on the basis of the Oxford Survey, an average prenatal risk factor throughout pregnancy of approximately 1.5, we estimate that prenatal x rays in any one year could result in approximately 19 extra cases of childhood cancer each year for the next 15 years. (Table 3). (As previously noted, one of these 19 extra cancers can be attributed to the use of prenatal x-rays during the first month of pregnancy. This risk estimate is also susceptible to the same uncertainty noted previously, namely validity of the assumption that the fetal doses in the Oxford Survey are comparable to those in the United States in 1970). Therefore, the estimated number of cancers due to irradiation at any time during pregnancy is 280 cases per year at equilibrium in children under 15 years of age.

Stated in individual terms, the cumulative probability that a child who was irradiated through a prenatal abdominal x-ray examination consisting of 2-3 radiographs will develop cancer during the first 15 years of life is about 1 in 1000. For individuals who receive larger doses, the estimated risk would be increased proportionately under the linear dose-effect model. For example, the radiation received by the embryo from a typical abdominal fluoroscopic procedure is many times greater than that from 2-3 radiographs. Thus, the 1 in 1000 risk estimate could be substantially increased.

It should be emphasized that these risk estimates, which are derived from the results of the Oxford Survey of Childhood Cancers, are subject to revision as medical radiation usage changes. Concerning radiation throughout all of pregnancy, Bithell and Stewart stated, "Analysis of the risk by year of birth shows a pattern of steadily declining risk for both solid and haematopoetic tumors; this may be partly attributable to lower radiation doses per film exposed but is also due to the smaller numbers of films used. A consequence may well be that the risk - always of small clinical significance - would become virtually undetectable in future investigations" (2) (Emphasis added.)

In addition to an increased risk of childhood cancer, prenatal irradiation during the last two trimesters may be associated with subtle mental, physiological, and genetic changes that are difficult to detect and measure. Also, other environmental stresses and the genetic character of an individual may modify the biological response to radiation. The human embryo and fetus have been shown to be particularly susceptible to a variety of chemicals, drugs, viruses and other physical agents. One or more of these agents could potentiate the effects of x rays, thus altering the foregoing risk estimates.

Table 3. Derivation of Estimated Annual Incidence of Childhood Cancers Resulting from Abdominal X-ray Examinations in Pregnant Women Through all of Pregnancy

	Annual Rates	Annual No. in U.S
Fetuses Irradiated from Abdom. Examinations		298,000
Childhood Cancer Cases:		
Natural Incidence	12.5/100,000	37
Exposed to X Rays	18.75/100,000 (a)	56
Increased Incidence Resulting from X Rays	6.25/100,000	19

(a) This rate corresponds to the naturally occurring rate (12.5/100,000) times the increased risk factor (1.5), assuming that the exposed women were given abdominal examinations averaging 2 to 3 x-ray films each, with fetal doses comparable to those in the Oxford Survey.

III. CLINICAL RECOMMENDATIONS ABOUT THE USE OF IONIZING RADIATION IN PREGNANCY : HISTORICAL DEVELOPMENT

Although clinical concern for the potentially deleterious effects of medical x radiation was expressed in the literature as early as 1901 (20), its teratological potential was not recognized until some time later. From the 1920's through the mid-1950's, ionizing radiation was used to treat a variety of benign diseases and included procedures that delivered therapeutic radiation to the female pelvis (9). During this period, published reports described developmental abnormalities in children who had been heavily irradiated as fetuses (9,20). Goldstein and Murphy (1929) reported a high incidence of developmental abnormalities (mainly microcephaly and other mental defects) in children irradiated with high doses of ionizing radiation while in utero. They concluded:

> It is our belief that therapeutic pelvic irradiation during pregnancy is extremely likely to seriously injure the growing embryo, and that such injury may result in the birth of a seriously defective child. (12)

In 1952, William and Liane Russell reported a series of experimental observations on the teratological effects of x radiation correlating gestational age at exposure with type of effect. Based upon their assessment of the literature and upon their own laboratory findings, they became concerned with the potential for damage of therapeutic and diagnostic radiological procedures on pregnant women. Consequently, they suggested that pelvic irradiation should be restricted to the two weeks following menstruation to minimize the chance of irradiating a woman during an unsuspected pregnancy (39). They concluded:

> In view of the observations reported, it is recommended that:
>
> (a) Whenever possible, irradiation involving the uterus in women of childbearing age should be restricted to the two weeks following the last menstrual period, to preclude the possibility of fertilization having taken place. This applies particularly to diagnostic irradiation, even if the doses involved are less than 25 r.
>
> (b) The present practice of avoiding irradiation during a known pregnancy, i.e., during later stages, should not be relaxed.
>
> (c) Whenever possible in non-pelvic irradiation, the conceptus should be shielded. (39)

In 1955, the Russells further explained the reasoning for their concern for the use of ionizing radiation during pregnancy and reiterated their original recommendation.

> Therapeutic irradiation of the pelvic region can involve doses which are high from the point of view of hazard to the embryo: and certain types of diagnostic irradiation, particularly those involving fluoroscopy, may fall into the dose range for which malformations can be produced with relative ease in the mouse.

> We have, therefore, recommended that, whenever possible, pelvic irradiation of women of childbearing age should be restricted to the two weeks following the menses as there is comparatively little chance of an unsuspected pregnancy during that time. (40)

The clinical recommendation made by the Russells to limit pelvic irradiation of women of childbearing age where possible to the two weeks following menstruation was echoed by a number of organizations and individuals. A review of the original 1960 Adrian Committee Report emphasized the importance of the menstrual history with reference to radiographic examinations of women.

> Special precautions should be adopted in the radiography of pregnant women. Only essential examinations should be carried out during pregnancy.
>
> A particular danger is the irradiation of the uterus in an early undiagnosed pregnancy; in general medical and surgical practice the possibility of pregnancy should be considered and inquiry made concerning the recent menstrual history of any woman of childbearing age before any abdominal radiological investigations or the use of radioisotopes are instituted. (30)

The International Commission on Radiological Protection (ICRP) published recommendations in 1964 on the use of radiological procedures involving the lower abdomen and pelvis of women of childbearing age. These recommendations limited the use of radiological examinations that are not essential to the patient's immediate health to the 10-day interval following the onset of menstruation.

> The Commission wishes to call attention to reports of embryonic and foetal sensitivity to ionizing radiation and to emphasize that the possibility of pregnancy must be taken into account by the attending physician when deciding on radiological examinations that involve the lower abdomen and pelvis of women of reproductive age. The Commission also wishes to point out that the 10-day interval following the onset of menstruation is the only time when it is virtually certain that women of such age are not pregnant. Therefore, it is recommended that all radiological examinations of the lower abdomen and pelvis of women of reproductive age, that are not of importance in connection with the immediate illness of the patient, be limited in time to this period when pregnancy is improbable. The examinations that should be delayed to await the onset of the next menstruation are those that could without detriment be delayed till the conclusion of a pregnancy or at least until its latter half (17).

This recommendation came to be known as "The Ten Day Rule" (47). In 1968, the National Council on Radiation Protection (NCRP) published its original recommendations based on a 10-day interval following the onset of menstruation:

> 2.4.3 Protection of the embryo or fetus during radiological examination or treatment of women known to be pregnant should be given special consideration.
>
> Comment: Ideally, abdominal radiological examination of a woman of childbearing age should be performed during the first few (approximately 10) days following the onset of menses to minimize the possibility of irradiation of an embryo. In practice, medical needs should be the primary factors in deciding the timing of the examination. (27)

In 1970, the ICRP published a report concerning the use of radiographic examinations in pregnancy which contained the following recommendations:

> (174) The ICRP has for a number of years called attention to the embryonic and foetal sensitivity to ionizing radiation. The possibility of pregnancy must be taken into account by the attending physician when deciding on examinations that involve the lower abdomen and pelvis of women of reproductive capacity. The Commission has pointed out that the ten-day interval following the onset of menstruation is the time when it is most improbable that such women could be pregnant. Therefore, it is recommended that all radiological examination of the lower abdomen and pelvis of women of reproductive capacity that are not of importance in connection with the immediate illness of the patient, be limited in time to this period when pregnancy is improbable. The examinations that it will be appropriate to delay until the onset of the next menstruation are the few that could without detriment be postponed until the conclusion of a pregnancy or at least until its latter half.
>
> (175) While pelvimetry is sometimes of great value, it should be undertaken only on the rare occasions when this is likely to be so and should never be carried out on a routine basis." (18)

In 1970, the ICRP published a Task group report containing additional commentary and recommendations about the use of radiological procedures during pregnancy:

> Patient protection during pregnancy is particularly important because radiological examinations of the abdominal region of a pregnant woman frequently result in whole body irradiation of the foetus. Such radiation may contribute to the incidence of childhood leukemia and foetal abnormalities. In addition, these examinations may contribute a substantial proportion of the genetically significant dose (see Table III). Non-radiological methods of examination may be preferable where they can give comparable information. While pelvimetry is sometimes of great value, it should be undertaken only on the rare occasions when this is likely to be so and should certainly not be carried out on a routine basis. In particular, the supero-inferior projection for the

> pelvic inlet (sometimes called the brim view) is to be discouraged, in view of the high doses delivered to the foetus.
>
> Where radiography is carried out, it is essential to reduce the beam size to the minimum and this may involve the use of specially shaped apertures (Section 4.03). In addition, it is frequently possible to obtain information of diagnostic value from films of low contrast, and this enables higher kV and filtration than usual to be used (Table V). High-speed films and screens are advocated. (19)

In 1971 the NCRP revised its original 1968 recommendations and included a 14-day interval instead of the original 10-day recommendation, which came to be known as "The Fourteen Day Rule."

> When radiological procedures are planned on pregnant or potentially pregnant women, special consideration must be given to the relatively high radiosensitivity of the fetus in utero, particularly during the early phases of gestation. It is recommended that radiologic examinations of the abdomen and pelvis which do not contribute to the diagnosis or treatment of such women in relation to their current illness (e.g., low back examinations for employment) be restricted to the first 14 days of the menstrual cycle in the case of potentially pregnant individuals and avoided entirely during known pregnancy. Examinations of other parts of the body may be done at any time provided such examinations are conducted under conditions carefully designed to limit radiation exposure to an amount necessary for an adequate examination. Filtration, collimation of the radiation beam to the anatomical region of interest and careful selection of technical exposure factors can significantly contribute to good radiation practice and the reduction of radiation exposure to all tissue.
>
> Examinations of the abdomen and pelvis that are deemed useful to patient care may be done at any time without

> regard for the phase of the menstrual cycle or fetal presence. In each case the final decision to proceed or not to proceed must reside with the attending physician, in consultation with the radiologist when such services are utilized; that is, the attending physician must retain full and complete discretion to decide each case according to his judgment. (28)

In 1972, recommendations published in the British "Code of Practice" offered guidance for radiological protection of the patient during pregnancy.

> 73.1 In all women of reproductive capacity the clinician requesting the examination should consider the possibility of an early stage of pregnancy. The date of the last menstrual period should be entered on the request form and it is the responsibility of the clinician requesting the examination to ascertain this. To reduce the likelihood of irradiation of a pregnancy, examinations involving the lower abdomen should, if practicable, be carried out within 10 days following the first day of the menstrual period.
>
> 73.2 Special precautions should be adopted in the radiography of women known to be pregnant. Only absolutely essential examination should be carried out during pregnancy and particular care should be taken to minimize irradiation of the foetus.
>
> 73.3 Mass miniature techniques should not be requested for chest examinations of pregnant women. Full-sized films with strict limitation of field size should be used for these examinations. (8).

In 1971, the Fourteen Day Rule and other measures designed to safeguard the unborn child from unnecessary prenatal irradiation were recommended in a joint 1971 publication by the American College of Radiology, Public Health Service and American Medical Association.

(c) PREGNANT WOMEN (AND WOMEN WHO MIGHT BE PREGNANT) The concern here is with the unborn child. X-ray procedures that include the uterus of women who are, or might be, pregnant require particular guidelines in selection and timing. Examinations of other parts of the body may be done at any time provided such examinations are conducted under conditions limiting the radiation exposure to the amount necessary for adequate examination.

In all women of childbearing age who may be pregnant, the period of choice for examinations involving the abdomen and pelvis is the first 14 days after onset of a menstrual period. In the remainder of the menstrual cycle of women who may be pregnant, the physician should consider whether he would still ask for the examination if the woman were known to be pregnant.

If the physician considers the examination necessary for immediate patient care, it should be conducted in accordance with good technical practice, even if the patient is pregnant. If he considers the examination useful but not necessary for immediate care, he should consider postponing it.

In the event that an examination is postponed because of the possibility of pregnancy, and the woman does prove to be pregnant, then a new decision is necessary as to whether further postponement is allowable. This situation is responsible for the recommendation that the only examinations which should be considered for postponement are those which could be further postponed until at least the latter half of pregnancy, without seriously compromising the proper medical care of the patient. The reason for such further postponement, if possible, is that the relatively higher radiosensitivity of the fetus is greater during the first trimester as compared to a later trimester of prenatal life.

> ### (d) A PRACTICAL POLICY OF X-RAY EXAMINATIONS OF PREGNANT WOMEN
>
> The need for an x-ray examination of abdomen and pelvis varies in its importance for the patient's benefit, and the physician must apply a broad scale of urgency, not susceptible to precise definition. At one extreme would be the example of a patient thought to be pregnant and who had relatively minor gastrointestinal or urinary tract symptoms of the type that frequently occur during pregnancy. In this case, there probably is not sufficient indication for a gastrointestinal examination or an excretory urogram. If, on the other hand, the patient has unexplained hematuria or melena, there would be adequate indication for proceeding with such a study, even in the case of confirmed pregnancy in the first trimester. In such circumstances, the radiologist should be informed of the pregnancy so that, if possible, the examination could be modified to reduce radiation dose to a level even lower than usual.
>
> If an x-ray examination is performed before the patient's pregnancy is discovered, there is normally little cause for concern. In most procedures, the radiation exposure is so small that the risk of interference with fetal development is negligible. Such radiation exposure alone should not be used as a justification for interruption of the pregnancy. In very unusual circumstances when it is suspected that a diagnostic procedure or combination of procedures may have resulted in an uncommonly large exposure, efforts should be made to determine the fetal dose, and experts should be consulted about the possible hazard. (49)

In addition to the recommendations of national and international radiation protection groups, other individuals and institutions have expressed their concern for the unnecessary use of ionizing radiation in pregnancy. Several selected viewpoints follow:

> Prior to pelvic radiation of women of childbearing age, the radiologist should ascertain the time of the last normal menstrual period and if there is a remote possibility of pregnancy. X-ray examinations involving the pelvis should be avoided whenever possible, and in spite of the statistical improbabilities, the safest procedure is to restrict pelvic radiation to the two weeks following menstruation.
>
> During pregnancy, roentgen studies of parts of the body other than the pelvis and lower abdomen are probably safe, since no direct rays reach the embryo and scattered rays are minimal. Even so, as an added precaution, the pelvic area should be shielded from accidental direct exposure by use of protective lead material. (1)

> In order to avoid irradiation of the conceptuses of undiagnosed early pregnancies, irradiation should as far as possible be performed only during the first half of the menstrual cycle. Women who are known to be pregnant should only be Roentgenologically examined on very strong clinical indications. (20)

> Radiodiagnosis and radiotherapy are absolutely essential to modern medicine. However, ionizing radiations are so potent and penetrating that the highly radiosensitive human embryo and fetus should be protected against any exposure if at all posssible, particularly during the first six weeks after conception. When the mother's health is in jeopardy, she must take priority over the fetus in any decision regarding the use of irradiation. (37)

In summary, a number of organizations and individuals have manifested their concern for protecting embryos from maternal medical radiation by recommending clinical protocols based in principle on the Russells' recommendations.

IV. DISCUSSION OF ELECTIVE SCHEDULING SYSTEMS

Some hospitals and other clinical facilities have instituted operating protocols based upon either the existing 10 or 14 day rules or modifications of them. These protocols, sometimes called "elective scheduling systems," call for the scheduling of non-emergency abdominal x-ray examinations of women of childbearing age during the first two weeks of their menstrual periods, when pregnancy is unlikely. For example, at Parkland Hospital in Dallas, Texas, patients are scheduled according to a "10-day rule" (high risk examinations) or a "28-day rule" (low risk examinations). Non-emergency high risk examinations (barium enemas, upper GI examinations, intravenous pyelography, etc.) are performed during the first 10 days of the menstrual cycle, while low risk examinations (radiography of the hips, abdomen, lumbar spine, etc.) are performed immediately, unless the patient is 28 days past her last menstrual period and hence late; in such cases the examination is postponed in consultation with the referring physician until the onset of menstruation (44).

This chapter will outline the major characteristics of elective scheduling systems, and discuss their benefits and limitations. In this regard, it is important to point out that two populations of women patients are inevitably involved in the practice of these systems. The smaller group consists of those patients who are actually but unknowingly pregnant; the larger group consists of those potentially pregnant women who are in fact not pregnant. The former group has embryos that might benefit from efforts to curtail abdominal x-ray exposure of their mothers; the latter group does not have viable embryos to benefit from such efforts. Consequently, analysis of the net public health benefits and limitations of elective scheduling systems must include the health implications not only to the embryos at risk but also to both sets of women patients involved.

Regardless of their differences, systems for scheduling abdominal area x-ray examinations for women of childbearing age generally have in common the following procedures, goals, and assumptions:

1. Patients are queried to determine the likelihood of their being pregnant. Scheduling of an examination to avoid irradiating an embryo is considered unnecessary (because pregnancy is unlikely or impossible) if any of the following conditions are discovered to exist:
    a. Menstruation has never occurred.
    b. Onset of menstruation occurred less than 10 (or 14) days before the examination is planned.

c. Menstruation has ceased because of menopause, hysterectomy, or oophorectomy.

d. Bilateral tubal ligation has been performed.

e. Birth control pills are taken regularly.

f. Intra-uterine device has been fitted.

g. Intercourse has not occurred since the last menstrual period.

h. The patient's husband has been vasectomized or is otherwise infertile.

2. In order to avoid the irradiation of a newly fertilized egg, elective scheduling systems are intended for patients who are not known to be pregnant, but who could be. In other words, these systems are intended for women who are in the post-ovulatory stage but who have not yet missed a menstrual period, i.e., those who could possibly be in the first two weeks of pregnancy. (The patient's actual pregnancy status will of course not be known to her or her physician.) As practiced at several U.S. medical facilities, the radiology department schedules the woman's abdominal x-ray examination during the time of her next expected menses. Pregnancy is not likely to occur during the menstrual period, so if her menstrual

period starts as expected, the examination is performed. If her menstrual period does not start, and if her medical condition still warrants the examination, then some alternative measures must be taken.

3. Scheduling systems are appropriate only for elective examinations. If, in the opinion of the referring physician, a patient's symptoms warrant an immediate radiological examination, it is performed immediately. This implies that any radiation damage to a potential embryo is considered to be less likely or less serious than the larger risk of medical harm to the woman if diagnosis and treatment are delayed, and the risk of consequent indirect harm to her child if her health is thus impaired. Each scheduling system depends upon a decision by a referring physician concerning whether or not the patient's symptoms warrant an immediate examination. The criteria applied by each physician in making this decision are in part objective and undoubtedly in part subjective and intuitive.

4. Scheduling systems are appropriate only for abdominal area examinations. Other diagnostic x-ray procedures do not contribute a significant dose to the embryo or

fetus, and with the application of appropriate technological precautions, can be performed at any time during pregnancy without appreciable risk to a developing child.

5. Scheduling systems rely on either the radiology department or the referring physician to screen female patients. In the latter case, the referring physician is usually required to enter the date of the last menstrual period on the x-ray referral slip.

Elective scheduling systems have several limitations.

1. The NCRP and ICRP scheduling recommendations specify that they are appropriate only for those examinations which, if the patient is found to be pregnant on the scheduled date of the examination, may be postponed to a later period of pregnancy or after delivery without significantly compromising the patient's medical care.

   These recommendations, in effect, require that the referring physician make a personal commitment. That is, he must decide when the patient is first seen that, if she is found to be pregnant at the time of her scheduled examination, the examination will be postponed until term or at least its latter half. This effectively limits the number of x-ray examinations which are appropriate for elective scheduling, because it is likely that in only a relatively few cases could a physician be reasonably sure that the patient's condition will not deteriorate, possibly forcing him to order the x-ray procedure whether she proves to be pregnant or not.

However, this important commitment is not made and followed in elective scheduling systems as they are practiced in some institutions. Although the ICRP recommendation states that few examinations qualify for the postponement to term, medical facilities have generally tended to include all non-emergency abdominal examinations in their elective scheduling protocols. Consequently, women may be scheduled for examinations for which postponement may be medically unjustified. As a result, for those women who are postponed to await the onset of menses, who are later discovered to be pregnant, but whose examination becomes necessary (i.e., no longer "elective"), the examination will be performed during the period of organogenesis, a time when the embryo is most sensitive to congenital malformations. This application of the Russells' recommendation may actually increase the risk they intended it to reduce, if the physician decides that the examination may not be further postponed in spite of pregnancy. It should be re-emphasized that this situation would theoretically not occur if the ICRP or NCRP rules were rigorously followed. These rules state that the only examinations which should be postponed are those few which are not related to the current illness of the patient - those predictably elective examinations which could safely be postponed until term or the latter part of gestation if the woman is in fact pregnant.

In those institutions where the NCRP and ICRP recommendations are followed as they were intended, the referring physician's judgment is paramount. In the usual course of events, only the referring physician has all the pertinent clinical facts (symptoms, history, other diagnostic findings, etc.) needed to decide whether a contemplated examination meets the strict criteria for scheduling and possible postponement.

2. Scheduling is of no direct benefit to those women who are not found to be pregnant after the postponement period, since they were also not pregnant when the physician first saw them, and therefore could have had the examination without delay. In fact, postponement of the x-ray examination for these individuals may have served only to delay their effective medical treatment. Of course, by the very nature of the problem, a referring physician could not have predicted whether a woman patient was actually pregnant or not when the decision to postpone an examination was made. However, the fact that a substantial proportion of women have nothing to gain from elective scheduling and may actually be at some medical risk from the delay, must be considered in the complete public health evaluation of these systems.

3. Certain patients may not return for the scheduled examination, and hence endanger their own health. Although it is true that in some cases the need for an x-ray examination may no longer exist by the time the patient is scheduled to receive it, it is not acceptable medical practice to arbitrarily postpone indicated diagnostic tests and appropriate treatment on the chance that some patients may improve without it.

4. The ICRP and NCRP recommendations and many clinical scheduling systems apply only to women who have menstrual flows of normal intensity occurring regularly every 28 days, and whose ovulation occurs at about mid-cycle and can thus be calculated with some certainty. The use of the 10- or 14-day rules to determine a safe period is not applicable in women with irregular cycles or women who menstruate more or less frequently than monthly. These women have about a 10 percent chance of ovulating during the first 10 days of their cycles and about a 50 percent chance during the first 14 days (3).

5. Scheduling systems rely on obtaining a reliable menstrual history from the patient, which, because of its personal nature or other factors, may be difficult to obtain accurately.

6. The ICRP, in advising that abdominal examinations be postponed at least until the latter half of pregnancy, has implicitly accepted the radiogenic risks which might accrue then, in trade for the risks in the first month of pregnancy. Following the rule does not eliminate all risk to the fetus, unless the examination is postponed until term. A judgment about acceptable risks might be more properly the province of the physician and the patient.

7. Scheduling systems relate only to the potentially pregnant patient and provide no advice on managing the patient who is known to be pregnant. Yet they are sometimes erroneously considered a comprehensive solution to the problem of medical radiation exposure of the fetus throughout gestation. We estimate that, in 1970, 276,000 fetuses were irradiated in the U.S. during the second and third trimesters, a time when the pregnancy is undoubtedly known. In the same year, only 22,000 fetuses were irradiated during the first trimester. Even if all the first trimester x-ray examinations met criteria for postponement, only 8% (22,000/276,000) of all irradiated fetuses could have been affected. It is clear that scheduling systems are not a comprehensive approach to all medical radiation exposure during pregnancy.

Scheduling systems do provide certain benefits.

1. They make physicians aware that x-ray exposure of the fetus may be harmful, and this awareness probably causes some physicians to rethink the need for an examination of a woman they suspect of being pregnant.

2. They may stimulate physicians to take more care in inquiring about the patient's pregnancy status.

3. They may eliminate some unneeded examinations because some patients will no longer be ill following the postponement period. However, this latter benefit may be counterweighted by those situations where postponement leads to a worsening of a medical condition.

HYPOTHETICAL CASES

The following hypothetical cases illustrate some advantages and disadvantages of scheduling women of childbearing age according to the "Ten Day Rule."

Case 1

Mrs. X, who is beyond the 10-day interval since the onset of menses, must be scheduled for an abdominal x-ray examination. She is given an appointment for a time during the 10-day interval following the onset of her next menses. Mrs. X has her next menses and receives her x-ray examinations. Mrs. X obviously was either not pregnant at any time since her last menses or, if she was pregnant, has unknowingly had a spontaneous abortion. She could have been scheduled at any time during that menstrual period without danger to a viable embryo. Consequently, her postponement benefited no one.

It is also possible that Mrs. X suffered some aggravation of her medical condition because of a delay in diagnosis and treatment of her condition caused by postponing the x-ray examination. It is also possible that the delay was inconsequential to her health.

Case 2

Mrs. Y, who is beyond the 10-day interval, must be scheduled for an abdominal x-ray examination during the ten day interval following the onset of her next menses. Mrs. Y's menses do not begin on schedule and she believes she is pregnant. Assuming that fertilization has occurred on the fourteenth day after the onset of her last menses, the embryo is now about two weeks post-conception and entering the period of early organogenesis. Mrs. Y's physician decides he still needs the examination despite her early pregnancy. (The examination has turned out to be one that the physician, contrary to ICRP and NCRP recommendations, could not safely postpone until term). The fetus is now irradiated during the period of organogenesis, when the risk of congenital malformations from x radiation is greatest. In this case, postponement placed the fetus at greater risk of congenital malformations than if the examination had been done earlier. (Of course, had it been performed earlier, another type of risk would have been involved, a small increase in the probability of embryonic death. There is no period during gestation when the embryo or fetus is completely free of any risks due to x-ray exposure.)

Case 3

Mrs. Z, who was scheduled for an abdominal x-ray examination during her next menses, recovers from her illness in the meantime. Her physician then decides he does not need the x ray procedure. In this case, postponement resulted in benefit to the patient by eliminating the risk and cost of an x-ray procedure.

Case 4

Mrs. W is found to be pregnant following postponement to await the onset of menses. Her physician decides to postpone the examination until after her child is born. Since the examination may be postponed for such a long period of time, it could be questioned whether the examination is needed at all. There is also a possibility that postponement may delay a correct diagnosis and thus adversely affect the mother's (and perhaps indirectly the child's) health. On the other hand, postponement until term does eliminate all exposure of the unborn child.

Clearly the only women who will menstruate after they are postponed are those who were not pregnant originally, (or who lost the embryo shortly after conception) and who therefore never had a viable embryo at risk. Except for spontaneous abortions, those who were pregnant stay pregnant. For these women, the physician faces the crucial decision of whether or not to proceed with the examination. As mentioned earlier, the embryo may have progressed to the period of major organogenesis, a particularly radiosensitive period in its development, when its risk of congenital malformation may be highest. Additionally, the mother's medical condition may have worsened.

V. BASIC PRINCIPLES AND ASSUMPTIONS FOR THE CLINICAL MANAGEMENT OF PREGNANT AND POTENTIALLY PREGNANT PATIENTS

Before considering an alternative course of action to existing scheduling systems, there are several underlying principles and assumptions which must be recapitulated. Any logical and biologically justified approach must take these into account.

1. Review and analysis of the pertinent literature supports the assumption that the developing embryo and fetus is subject to various radiological risks. The kind and degree of risks vary depending upon the precise embryonic age at which the radiation is delivered, a number of biological and environmental variables, and a number of physical factors such as the quantity, type, energy, and spatial and time distributions of the radiation involved.

2. It is prudent to assume that no amount of medical x-ray exposure to the embryo and fetus is completely without effect at any time during pregnancy; the earlier part of pregnancy appears to be somewhat more susceptible to radiogenic risks than later stages.

3. Primary care physicians have the dual responsibility to provide appropriate medical care for their patients as

well as to be cognizant of radiological risks and to take them into account in their patient care decisions. It should be pointed out that the physician is primarily responsible to the patient and secondarily to the fetus or embryo. This is one of the underlying assumptions on which both the ICRP and NCRP recommendations are based. This is especially important when the physician has to consider the health benefits from the examination to the patient versus the risk to the embryo or fetus of a potentially pregnant patient.

4. Expert organizations and governmental agencies can play an important role through the development and dissemination of scientific information which can aid the physician's decision making, but only he or she can competently make the final decision about the necessity for or timing of an x-ray examination. The competing concerns of protecting mother and embryo or fetus from radiogenic risks, and providing the needed medical care, must be properly balanced by the patient's physician and not by remote parties, in order that one concern is not given inordinate weight at the expense of the other.

The alternative system for radiological management of pregnant or possibly pregnant women, a pregnancy awareness system for referring physicians, which is discussed in the following section, fulfills all of the above criteria.

VI. A CLINICAL APPROACH FOR THE MANAGEMENT OF PREGNANT AND POTENTIALLY PREGNANT PATIENTS - AN ALTERNATIVE FOR CONSIDERATION

Given the foregoing principles and assumptions, the following alternative system to elective scheduling is suggested for consideration. It emphasizes the collective responsibilities of referring physician, patient, radiologist, and x-ray equipment operator. This alternative system can effectively fulfill the primary goal of the 10 or 14-day rules, which is to avoid the unintentional irradiation of a newly fertilized egg, and can at the same time minimize several major drawbacks inherent in elective scheduling.

A. Referring Physicians

The referring physician is the most important person with respect to the irradiation of a pregnant or potentially pregnant patient. The referring physician by an x-ray request, initiates the process which culminates in the x-ray exposure of the patient, and possibly an unborn child. As will be discussed below, radiological personnel can take measures to keep the exposure to a necessary minimum, but the referring physician must decide whether or not it is needed at all. There have been reports of incidents where physicians have referred pregnant and potentially pregnant patients for allegedly unnecessary x-ray examinations (the implication being that reasonable care exercised in ordering these x-ray examinations would have led to their elimination), but the solution of such a problem is beyond the scope of any existing practical clinical protocol. This paper must start with the assumption that the physician is requesting an x-ray examination only after due consideration of its necessity in the treatment of the patient.

Unless the situation is of such an emergency nature that the information would be irrelevant, the physician should ascertain the likelihood that the patient is or may be pregnant. This is identical to the procedure described in Chapter IV,, Item 1 (p. 27). One method which has been suggested and used in some institutions to assure that referring physicians invariably ascertain the pregnancy status of the patient, when appropriate, is the annotated referral slip. On the referral request itself, appropriate space is provided for the referring physician to indicate: whether the patient is, is probably not, or may be pregnant; whether or not the examination should be performed irrespective of pregnancy status; whether he would like to consult the radiology department about the possibility of modifying the requested examination; or whether the examination should be postponed for a time. In some institutions, a space is provided on the referral slip for the referring physician to note the date of the patient's last menstrual period (LMP). The referral slip can be a permanent record of the consideration of pregnancy if it is appropriately filed and can be retrieved.

Whether or not the annotated referral slip can be an effective tool in assuring that referring physicians ascertain the possibility of pregnancy depends upon how vigorously the radiology department insists that referring physicians complete all parts of the referral slip and sign it.

When, as a result of this first step, the referring physician either suspects the possibility of pregnancy in the patient being considered for an abdominal-area x-ray examination, or knows she is pregnant, the second step is to make one of the following choices:

1. proceed with the referral as indicated; or
2. cancel the referral; or
3. consult with a radiologist regarding the advisability of either modifying the extent of the examination or referring the patient for a non-ionizing radiation examination, such as an ultrasound procedure; or
4. postpone the examination until the patient's next expected menses (in the case of a potentially pregnant patient), with the intention of further postponing the examination until term if she is found to be pregnant; or

5. postpone the examination until term (in the case of a patient known to be pregnant); or
6. postpone the examination for a time less than term (in the case of a patient known to be pregnant).

These options are discussed below.

1. Proceed with the referral

This option is an expression of those situations when the woman's medical circumstances dictate the need for an examination, regardless of whether or not she is pregnant. All the aformentioned clinical scheduling recommendations and protocols allow for the referring physician to bypass the scheduling system in emergencies or for immediate needs. Many examinations which are performed fall under this category. Only when the patient's medical circumstances allow the physician some latitude can other options be considered.

2. Cancel the referral

The referring physician may decide to cancel a contemplated examination, once aware of the possibility of pregnancy. The potential health benefit from a contemplated examination can be expected to be variable, and this will depend to a large extent upon the referring physician's conviction of its necessity. If the physician is very certain of its necessity, then the probability or actuality of a pregnancy would not dissuade the referral. If, on the other hand, there is less certainty of its necessity, then it is not unreasonable to assume that in some cases the examination may not be ordered, once the physician becomes aware of the probability or actuality of pregnancy. Of course, physicians should not be motivated either way by an unrealistic notion of the risks involved to the fetus and to the mother.

3. Consult about modification

Under certain clinical circumstances, an x-ray examination involving fewer exposures than routine may be tailored by the radiologist to provide the minimum necessary clinical information (i.e. less information than the routine procedure would provide) with less x-ray exposure. Whether such practices can prove to be in the best interests of the mother's and child's health currently remains controversial and probably should be decided on an individual basis. Some eminent radiologists have asserted that standardized exams have been designed to provide the optimum information and any less would entail a health care penalty. Others have disagreed and routinely modify examinations to suit individual circumstances. The referring physician should be encouraged to seek the advice of a radiologist or other clinical expert in radiological interpretation concerning this issue.

Various ultrasound procedures are replacing or supplementing certain x-ray examinations. The referring physician should realize that it is not yet known whether diagnostic ultrasound conveys biological risks, and he should be vigilant for such information appearing in the medical literature. However, he may wish to consult with a radiologist about the advantages and limitations of these procedures where certain information required might be obtained by ultrasound techniques.

Postponing Exams

Postponable examinations have been the subject of a continuing controversy, and there are several central issues which require discussion. First, postponement of a needed examination for any appreciable length of time involves a health risk to the patient. That is, there is a risk that a radiologically diagnosable condition will worsen during the postponement interval, while proper and effective treatment may have been delayed. This risk must be evaluated and weighed against the reduction of risks to the unborn child because of postponement.

Second, there are two generic kinds of postponement, postponement for a time less than term and postponement until term. Postponement until term results in the abdominal x-ray examination being delivered only to the mother, while the baby receives no exposure. The mother's ovaries receive some x-ray dose, so that there may be potential effects to her future children; but assuming that the examination must be performed at some time or another, postponement will not alter this fact. Postponement for a time less than term results in both mother and child being irradiated. Although postponement causes the exposure to be given at a later gestational age, regardless of when during gestation it is irradiated, the fetus incurs some biological risk; however, the magnitude and type may vary.

4. Postpone the examination until her next expected menses

This option, essentially the 10-Day or 14-Day Rules of the ICRP and NCRP, emphasizes the lengthy postponement required if the patient is found to be pregnant. It has not been established whether any examinations exist which should be performed and which unequivocally can be safely postponed for several months without detriment to the patient's medical well-being. Nevertheless, this option exists as a logical alternative course of action for those physicians who feel their patient's circumstances fit the restricted criteria. As explained earlier; postponement of examinations which the physician would not be willing to postpone until term or until the latter part of gestation if the woman is found to be pregnant, may result in more risks to the patient and her possible child than are avoided.

5. Postpone the examination until term

Option (5) is postponement until term for those known pregnant patients whose medical well-being would not suffer by delay of diagnosis and treatment, in the considered opinion of the referring physician. The arguments for and against this option are similar to those given for Option (4). Of course, depending upon when during a particular patient's pregnancy the issue arises, the delay involved may be days or months long, and the medical risks from the delay might vary accordingly.

6. Postpone the examination until later in gestation

Postponement of an abdominal x-ray examination of a known pregnant patient for a time less than term, Option (6), results in x-ray exposure to both mother and fetus as previously mentioned. Since the fetus is exposed at a time later in gestation than it would have been without postponement, the kind and magnitude of biological risks to which it is subject may be different. However, there appears to be no time during gestation when the embryo and fetus can be exposed to x radiation without any risk of some biological effect.

It is not unreasonable for a physician to delay ordering an x-ray examination on a pregnant woman, if the need for the examination is questionable at the time, if he feels there is an excellent chance that the woman's condition will improve spontaneously, and if he believes the possibility of adverse consequences from delay is remote. If her symptoms are not indicative of a serious acute condition which requires prompt treatment, and if the condition will likely improve without the examination, a delay could be medically justified and would have the side benefit of sparing the fetus from x-ray exposure. It is not clear how often these restricted circumstances might occur, but the alternative should be available to the physician/patient as a matter of principle.

B. Patients, radiologists, and x-ray equipment operators

Participation in avoiding medical x-ray exposure of the human embryo and fetus involves more persons than the referring physician. The x-ray examination process involves three main processes: the determination that a patient will undergo the examination, the conduct of the x-ray examination, and the interpretation of the examination results. The referring physician is indeed involved in the first stage; however, even at this stage, a second party, the patient herself, has a key role to perform.

The simplest, but most important, task she can do is inform the referring physician if she suspects or knows that she is pregnant. She should also inform her physician about any previous x-ray examinations she has had. This examination history may be beneficial in eliminating the need for some examinations, if a recent examination can provide the information needed. Finally, knowing that she is scheduled to receive an x-ray examination of the abdominal area, the patient should postpone a planned pregnancy until after the examination.

The person, usually a technologist, who performs the x-ray examination is instrumental in determining the dose received by the patient and hence the embryo or fetus. It is beyond the scope of this Technical Overview to discuss in detail all the factors which should be considered by the operator in properly performing an x-ray examination. However, a few points should be stressed. Before performing an abdominal area examination on a woman who is or may be pregnant, the operator should ask her whether or not she suspects she may be pregnant. In those situations where the patient is or may be pregnant, the operator should notify the physician in charge, usually a radiologist, before performing the examination.

The x-ray exposure of any patient should be kept to a necessary minimum in the performance of an x-ray examination by use of proper technique factors, proper film-screen combinations, collimation to the area of interest, and the other well-known factors involved in quality radiologic technology. A facility quality assurance program can be important in reducing the need for repeat examinations and hence in avoiding unnecessary radiation exposure. However, these procedures are especially important when a pregnant woman is given an x-ray examination, because a developing embryo is being exposed as well as an adult.

Although not directly associated in time with this stage of the examination, as previously discussed, the referring physician can influence the conduct of the examination by consulting with the radiologist about the patient's pregnancy and clinical history. The radiologist, based upon the referring physician's needs, can then advise on the feasibility of modifying the examination to reduce fetal exposure and determine the procedures to be followed by the machine operator during the conduct of the examination. Based upon the particular examination and the clinical needs, the radiologist may also provide guidance concerning the use of fetal shielding.

The radiologist also has the responsibility for the final stage of the examination process, that of analyzing the results. It is incumbent upon him to provide feedback to the referring physician and the machine operator to improve their practices, if necessary. For example, should he observe an unsuspected fetus in the field of view, the radiologist should notify both the referring physician and operator to increase their awareness of the need to ask female patients about their pregnancy status prior to the ordering and performance of abdominal x-ray examinations. Through this feedback process, the radiologist can influence the future actions of both referring physicians and x-ray technologists.

VII. Discussion

The clinical approach under consideration here differs from existing programs in three important respects: (1) it emphasizes that each patient's case should be handled individually (i.e. no single rule is applicable to all patients); (2) it discusses procedures which are applicable throughout pregnancy, not just during the first month; (3) it emphasizes the responsibilities for all parties concerned - the patient, the referring physician, the radiologist, and the x-ray equipment operator.

On the basis of the discussion presented in this Technical Overview, two realizations become apparent. First, the referring physician's judgment is the critical key to any efforts to reduce unnecessary medical x-ray exposure to fetuses, since it is the decision of the referring physician which places an individual into the x-ray examination process. There is no satisfactory way of avoiding that role without causing undesirable medical consequences, nor can the rules imposed by remote parties be expected to alleviate more risk of undesirable consequences than they may cause. The referring physician's judgment has always been important, even where elective scheduling has been practiced. The promulgation of elective scheduling recommendations and their practice in certain institutions may have tended to obscure the fact that referring physicians must choose between several alternative courses of action, no one of which is universally appropriate for all pregnant and possibly pregnant patients.

Second, the referring physician cannot claim to have considered all pertinent aspects of the patient's condition when ordering an examination (or, for that matter, a drug), unless some effort has been made to inquire whether the patient is or may be pregnant. Nor can the physician adequately weigh the merits of the other options without this information.

Once the referring physician has made a decision to proceed with an examination, the patient, the radiologist, and the x-ray machine operator all play vital roles in keeping the subsequent exposure to a minimum. Although redundancies appear in the system, they serve a useful purpose in insuring that the process is effective.

In summary, when considering abdominal x-ray examinations for a female patient of childbearing age, the referring physician should take positive steps to ascertain and document whether the patient may be pregnant. He should also possess a realistic understanding of the nature and degree of the risks to the developing embryo from diagnostic radiological procedures. With this information, the physician can choose between the available courses of action with respect to the woman's and the potential child's health care. Proper conduct of the examination, feedback of information to the referring physician and machine operator, and actions the patient can take are also important in improving the total patient management process. These steps collectively appear to be a more suitable response to the complexities involved in the radiological care of pregnant and potentially pregnant patients than elective scheduling routines.

References

1. Bishop, P. Teratogenic Effects of Radiation, Clinical Obstetric Gynecology 9: 631-640 (1967).

2. Bithell J. and A. Stewart, Prenatal Irradiation and Childhood Malignancy: A Review of British Data from the Oxford Survey, Br. J. Cancer 31:271-278 (1975).

3. Boice, J. and R. Burnett. Considerations of Possible Pregnancy in the Use of Diagnostic X Rays. Presented at Health Physics Society 7th Mid Year Topical Symposium, San Juan, Puerto Rico, (December 11-14, 1972). DHEW Publication (FDA) No. 73-8029 (1973).

4. Brent, R. and R. Gorson, Radiation Exposure in Pregnancy. Current Problems in Radiology 11:5 (Sept.-Oct., 1972).

5. Bross, J. and N. Natarajan. Leukemia from Low-Level Radiation: Identification of Susceptible Children. The New England Journal of Medicine 287:107-110 (1972).

6. Brown, R., J. Shaver and D. Lamel. A Concept and Proposal Concerning the Radiation Exposure of Women. Radiological Health Sciences Education Project, University of California, San Francisco Medical Center (1974); unpublished contract report.

7. Brown, R, Personal Communication (Jan. 1976).

8. Code of Practice for the Protection of Persons Against Ionizing Radiation Arising from Medical and Dental Use, H.M.S.O. London (1972).

9. Dekaban, A. Abnormalities in Children Exposed to X Radiation During Various Stages of Gestation: Tentative Timetable of Radiation Injury to the Human Fetus, Part I. Journal of Nuclear Medicine, 9: 471-477 (1968).

10. Diamond, E., H. Schmerler, and A. Lilienfeld. The Relationship of Intra-Uterine Radiation to Subsequent Mortality and Development of Leukemia in Children. American Journal of Epidemiology 97:283-313 (1973).

11. Division of Biological Effects, Bureau of Radiological Health (FDA), The Effects of Ionizing Radiation on the Developing Embryo and Fetus. Staff Document, (In Preparation).

12. Goldstein, L. and D. Murphy. Etiology of the Ill-Health in Children Born After Maternal Pelvic Irradiation, American Journal of Roentgenology, 22: 322-331 (1929).

13. Graham, S.,M. Levin, A. Lilienfeld, I. Schuman, R. Gibson, J. Dowd, and L. Hempelmann, Preconception, Intra-uterine, and Postnatal Irradiation as Related to Leukemia. National Cancer Institute Monograph 19: 347-371 (1966).

14. Hardin, G. Birth Control. Western Publishing Company, Pergasus, N.Y. (1970).

15. Harris, R. Viral Teratogenesis: A Reveiw with Experimental and Clinical Perspectives. American Journal of Obstetrics and Gynecology 119: 996-1008 (1974).

16. Hicks, S. and C. Amato. Effects of Ionizing Radiation on Mammalian Development. Advances in Teratology 1: 195-250 (1966).

17. International Commission on Radiological Protection. Radiation Protection, Recommendations of ICRP (1962 Revision), ICRP Publication 6. Pergamon Press, New York (1964).

18. International Commission on Radiological Protection. Committee 3 Report on Protection Against Ionizing Radiation from External Sources, ICRP Publication No. 15. Pergamon Press, New York (1970).

19. International Commission on Radiological Protection. Protection of the Patient in X-ray Diagnosis (adopted 1969), ICRP Publication 16. Pergamon Press, New York (1970).

20. Jacobsen, L. Low-Dose X-Irradiation and Teratogenesis, A Quantitative Experimental Study with Reference to Seasonal Influence on Dose Rate. Acta Pathologica et Microbiologica Scandinavia Supplementum, 193: 1-20, 151-159 (1968).

21. Kameyama, Y. Experimental Study on Developmental Anomalies Produced by X-Radiation. Acta Pathologica Japonica, 1: 1-16 (1959).

22. MacMahon, B. Prenatal X-ray Exposure and Childhood Cancer. Journal of the National Cancer Institute 28: 1173 (1962).

23. Milkovich, L. and B. VanDenBerg. Effects of Prenatal Meprobamate and Chlordiazepoxide Hydrochloride on Human Embryonic and Fetal Development. New England Journal of Medicine 291: 1268-1271 (1974).

24. Myers M., J. Young, E. Silverberg, and H. Heise. Cancer Incidence Survival and Mortality for Children Under 15 Years of Age. American Cancer Society Publication No. 3022 PE (1974).

25. Natarajan, N. and I. Bross. Preconception Radiation and Leukemia. Journal of Medicine 4: 276-281 (1973).

26. National Academy of Sciences, National Research Concil. The Effects on Populations of Exposure to Low Levels of Ionizing Radiation. (BEIR Report), Washington, D.C. (1972).

27. National Council on Radiation Protection and Measurements. Medical X ray and Gamma Ray Protection for Energies up to 10 MeV. NCRP Report No. 33, Washington, D.C. (1968).

28. National Council on Radiation Protection and Measurements. Basic Radiation Protection Criteria. NCRP Report No. 39 Washington, D.C. (1971).

29. Ohzu, E. Effects of Low-Dose X Irradiation on Early Mouse Embryos. Radiation Research, 26: 107-113 (1965).

30. Radiation Protection Committee of the British Institute of Radiology. Memorandum on Implementation of the Second Report of the Adrian Committee on Radiological Hazards to Patients. British Journal of Radiology 37: 559-561 (1964).

31. Rugh, R. and E. Grupp, Exencephalia Following X-Irradiation of the Pre-Implantation Mammalian Embryo. Journal of Neuropathology and Experimental Neurology, 18: 468-481 (1959).

32. Rugh, R. and E. Grupp, Effects of Low Level of X Irradiation on the Fertilized Egg of the Mammal. Experimental Cell Research, 25: 302-310 (1961).

33. Rugh, R. and E. Grupp, Neuropathological Effects of Low-Level X Irradiation of the mammalian Embryo. Military Medicine, 126: 647-664 (1961).

34. Rugh, R. Low-Levels of X Irradiation and the Early Mammalian Embryo. American Journal of Roentgenology, 87: 559-565 (1962).

35. Rugh, R. Can the Mammalian Embryo be Killed by X-Irradiation. Journal of Experimental Zoology 151: 227-243 (1962).

36. Rugh R., M. Wohlfromn, and A. Varma, Low-Dose X-ray Effects on the Precleavage Mammalian Zygote. Radiation Research, 37: 401-414 (1969).

37. Rugh, R. X ray Induced Teratogenesis in the Mouse and its Possible Significance in Man. Radiology 99: 433 (1971).

38. Rugh R., and W. Leach, X-ray Effects on the Embryo and Fetus: A Review of Experimental Findings. Presented at International Radiation Protection Association, Washington, D.C. (Sept. 9-13, 1973).

39. Russell, L. and W. Russell, Hazards to the Embryo and Fetus. Radiology 58: 369-376 (1952).

40. Russell, L. and W. Russell. Hazards to the Embryo and Fetus from Ionizing Radiation, Proceedings of the First International Conference on the Peaceful Uses of Atomic Energy, Geneva Switzerland 11: 175-178 (1955).

41. Russell, L. Effects of Low Doses of X rays on Embryonic Development in the Mouse. Proceedings of the Society of Experimental Biology and Medicine, 95: 174-178 (1957).

42. Stewart, A., J. Webb, and D. Hewitt. A Survey of Childhood Malignancies. British Medical Journal 1: 1495 (1958).

43. Stewart A., and G. Kneale. Radiation Dose Effects in Relation to Obstetric X rays and Childhood Cancers Lancet 1: 1185-1188 (1970).

44. Timing X rays to Protect the Embryo. Medical World News 708, (Nov. 3, 1972).

45. Uchida, I. and E. Curtus. A Possible Association Between Maternal Radiation and Mongolism. Lancet 11: 848-850 (1961).

46. Uchida, I., Maternal Radiation and Chromosomal Aberrations. Lancet 11: 1045-1049 (1968).

47. Warrick, C. Radiology Now. The "Ten-Day Rule", British Journal of Radiology 46: 933-934 (1973).

48. Wilson, J. Differentiation and the Reaction of Rat Embryos to Radiation. Journal of Cellular and Comparative Physiology, (Suppl.) 43: 11-37 (1954).

49. X-ray Examinations...A Guide to Good Practice. Prepared by the American College of Radiology, Public Health Service and American Medical Association. U.S. Government Printing Office, Washington, D.C. 20402 No. 5505-003 (1971).

X Rays And Pregnancy

The potential risk involved in an x ray administered to a pregnant woman depends on a variety of factors. The decision whether to order an x ray should be left to the physician, but a woman who is pregnant—or thinks she might be—can take steps that may help avoid an unnecessary x ray or reduce exposure if an x ray is advisable.

by James L. Morrison and Mark Barnett

A great deal of public concern has developed during the past few years over the possible hazards of x rays administered during pregnancy. Some magazine and newspaper articles have exaggerated the risk to the extent that they may have caused an unwarranted fear of x-ray examinations. Others have discounted the risks almost completely, implying that there is nothing to be concerned about.

Whether there is a risk and, if so, the extent of the risk, depend on a number of factors. One important factor, for instance, is the part of the body being x rayed. Properly performed x-ray procedures in which the mother's abdomen is not in the direct x-ray beam, such as examinations of the head, neck, teeth, chest, arms, and legs usually deliver almost no radiation to the unborn child.

Examinations in which the child lies within the direct x-ray beam expose it to considerably more radiation, particularly when a fluoroscope is used. Such examinations include x rays of the lower digestive tract, the urinary tract, lower abdomen, lower back, or hip area.

When there is a risk, the type and extent of the hazard depend on the amount of radiation and when during the pregnancy the exposure occurs. If a woman receives a radiation dose far in excess of that normally used for diagnostic x-ray examinations it can cause death of the developing embryo, which results in spontaneous abortion. This risk is greatest when the radiation is received very early in pregnancy—during about the first 9 days after conception. Such spontaneous abortions, however, probably cannot be produced by the levels of radiation usually used in ordinary diagnostic x-ray examination.

Tests with animals have shown that when high doses of radiation are administered during pregnancy the risk of major malformations in the offspring is increased. This risk is greatest during the stage of pregnancy when the various body organs are being formed which, in humans, is the second through the seventh week of pregnancy. During this period the developing embryo also is most sensitive to other agents that can cause malformations, such as drugs and viruses. It is generally agreed, however, that malformations are very unlikely to occur in unborn children as a result of exposure to ordinary diagnostic x rays.

The risk of malformations as a result of radiation exposure greatly diminishes after the eighth week of pregnancy. Other risks may be associated with exposure later in pregnancy, however. Evidence from studies of atomic bombing survivors and other groups suggests that large doses of radiation received during the later stages of pregnancy can produce severe effects on the behavior and intelligence of the child through damage to the central nervous system. The children of Japanese women who were exposed to atomic radiation during pregnancy showed more of a tendency to suffer severe mental retardation than the children of mothers who had not been exposed. But radiation doses to these women and fetuses were much higher and of a different type than those generally used in x-ray diagnosis, and it is unlikely that diagnostic x-ray procedures could produce profound retardation.

Information from animal studies suggests that smaller doses of radiation than those received by the Japanese survivors could produce slight effects on intelligence or behavior which would be very difficult to measure. It is not known whether these kinds of subtle effects might occur as a result of diagnostic x-ray exposures.

Several studies indicate there is an increased risk of leukemia and other cancer among children exposed to radiation as a result of abdominal x-ray examinations of their mothers during pregnancy. Although precise estimates of risk are not possible, the results of several studies indicate that the possibility of a child developing cancer before 15 years of age as a result of the radiation would be around one in a thousand, assuming a typical two- or three-film x-ray examination was made of the mother's abdomen. The likelihood would obviously increase somewhat if the examination involved more radiation, as with the use of the fluoroscope.

In light of these findings, should a physician order an x ray of the abdomen for a woman who is, or might be, pregnant? The answer is yes, if the physician decides that an x ray is necessary to protect the health of the mother. In this case, the medical benefits would outweigh the risks.

On the other hand, any unnecessary abdominal x-ray exposure of a pregnant woman should be avoided. The physician should be able to explain the reasons for an x-ray examination and why it cannot be postponed until after the baby is born.

Considering the unlikely probability of harm, a woman who has received an abdominal x-ray examination before she or her physician knew she was

*U.S. GOVERNMENT PRINTING OFFICE: 1978-241-181/82

FDA Consumer
REPRINTED FROM MAY 1977

HEW Publication No. (FDA) 78-8046

U.S. DEPARTMENT OF HEALTH,
EDUCATION, AND WELFARE
Public Health Service
Food and Drug Administration
Office of Public Affairs

The decision whether an abdominal x ray should be ordered for a woman who is pregnant or thinks she might be should be left to the physician. If an x ray is ordered, the physician should be able to explain the reasons for it and why it cannot be postponed until after the baby is born.

pregnant should not be alarmed. Indeed, the undue anxiety could be more harmful to the health of the mother and child than the x rays themselves.

There are rare situations early in pregnancy, before a woman or her physician knows that she is pregnant, when a woman may receive considerably more than the usual amount of radiation exposure. For example, the woman may have received a number of abdominal x-ray procedures over a short period of time, or she may have received radiation therapy for the treatment of a disease. Under these circumstances, the woman should discuss the possible risks with her physician.

FDA is developing guidelines on medical radiation exposure of women of childbearing age which include the recommendation that physicians determine whether a patient is pregnant before ordering x rays. In addition, a woman can take certain steps to minimize radiation exposure to her unborn child if she is pregnant or suspects that she might be:

- She should tell her physician if she is pregnant or thinks she might be so the physician can determine whether to order the x ray, cancel the examination, modify it to reduce the amount of exposure, or use a different type of diagnostic test.
- She should tell her physician about any similar x-ray examinations that she may have had recently. The physician may decide not to order a new examination, depending on when the last one was made and how it relates to the patient's present medical condition.
- She should inform the x-ray technologist (the person who takes the x rays) or the receptionist about her pregnancy before the examination so that protective measures can be taken.
- During the examination she should ask the technologist whether all necessary precautions have been taken to insure that the unborn child's radiation exposure will be as low as practicable.

If a woman who is not pregnant has an x-ray examination of the abdominal or pelvic areas she should try to avoid getting pregnant for at least a month after the examination.

One thing a woman, or any patient, should not do is to ask for an x-ray examination. That decision should be left to the physician.

James Morrison and Mark Barnett are with FDA's Bureau of Radiological Health.

Mr. ROGERS. As I see it, this information goes more to the patient than the doctor.

Mr. VILLFORTH. That is correct.

Mr. ROGERS. I am talking about getting to the doctor, the man who order it. I would hope you would follow up with the various specialties to make sure they are getting out the word to their members not just to put a sign in their office and then when the doctor says to the patient, go take an exam, she is probably going ahead and taking it, I would think. It seems to me we might have an immediate reaction in getting to the specialists who will deal in this, I would think.

Dr. KENNEDY. My feeling, Mr. Chairman, is that these represent very positive steps. We are undertaking these only after the kind of consultation these physicians regularly have among themselves at annual meetings has taken place. I would be surprised if any practitioner in that college is not aware of this program. But I agree, there should be systematic efforts to record and to measure that kind of communication among practitioners, and we will try to provide it for you.

Mr. ROGERS. Here is what I am saying, Mr. Commissioner: that unless the colleges get involved, they may think some of this information put out by HEW doesn't have too much validity. I have even heard that from the professions. So maybe what I am saying is if we will have a direct follow-up with those professional groups, it might be helpful rather than just having an informational card to the public.

Dr. KENNEDY. The poster that is on display in the doctor's office, in the obstetricians' and gynecologists' offices, is distributed jointly by the Food and Drug Administration and the American College of Obstetricians and Gynecologists. They were willing to have their name printed on the same piece of paper with us.

Mr. ROGERS. That is a step forward, and I commend you. If you will follow up now with them to see exactly what they are doing with their members, I think it would be helpful.

Dr. KENNEDY. Yes, sir.

Mr. Chairman, could I ask your consideration in rectifying an oversight?

Mr. ROGERS. Certainly.

Dr. KENNEDY. I rushed and forgot to introduce for the record a report we wanted very much to get into the hearing record on the enforcement of the diagnostic x-ray performing standard under the Radiation Control for Health and Safety Act.

Mr. ROGERS. Without objection, it will be made a part of the record.

[Testimony resumes on p. 428.]

[The following information was received for the record:]

ENFORCEMENT OF THE DIAGNOSTIC X-RAY PERFORMANCE STANDARD UNDER THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT OF 1968

JUNE 1978

Prepared By
DIVISION OF COMPLIANCE
BUREAU OF RADIOLOGICAL HEALTH
FOOD AND DRUG ADMINISTRATION

INTRODUCTION

This report will describe the current activities of the Food and Drug Administration's Bureau of Radiological Health to carry out the requirements of the Radiation Control for Health and Safety Act as it applies to diagnostic x-ray equipment. The provisions of the Act and the Regulations published subsequent to it will be discussed. Areas of concern in the enforcement of the diagnostic x-ray standard and possible solutions will be discussed.

SCOPE OF THE ACT

The Radiation Control for Health and Safety Act, Public Law 90-602, became effective on October 18, 1968, after more than 14 months of extensive hearings involving numerous representatives of government, industry, and the public. Its passage marked the beginning of a new era in the relationship between Federal health authorities and the electronic products industry.

The provisions of the Act apply to all electronic products manufactured or assembled within or imported into the United States and its territories on or after October 18, 1968. The term "electronic product" can be briefly defined as any manufactured electronic device which can affect the emitted radiation. "Electronic product radiation," as defined by the Act, includes both ionizing and nonionizing electromagnetic and particulate radiation as well as sonic, infrasonic, and ultrasonic waves. The broad scope of these definitions is necessary in order to cover effectively the wide range of complex, radiation-emitting electronic products that are commercially available for consumer, medical, industrial and research applications. Because most radiation sources used by industry are electronic products, the Act has a direct effect on the manufacturers of these products.

The primary responsibility for implementing and enforcing the provisions of the Act has been delegated to the Food and Drug Administration's Bureau of Radiological Health. This responsibility entails the establishment of an electronic product radiation control program that involves both formal regulatory activities and a variety of efforts in basic research and development. The law specifically directs the Secretary of HEW to study the conditions of exposure to electronic product radiation and the resulting biological effects. The Bureau also has established and is maintaining liaison with interested persons both inside and outside of government and is supporting research and training in methods of minimizing unnecessary exposure to electronic product radiation. While these general activities are of considerable importance in their own right, they are intended primarily to support the central purpose of the law, which is to regulate and control the emission of electronic product radiation which represents a hazard to human health and safety.

The principal regulatory authorities provide the Bureau of Radiological Health the power to require manufacturers of electronic products to correct any defects relating to the (radiation) safety of use of their products, and the authority to establish and enforce radiation safety performance standards for specific types of electronic products. These are the main regulatory powers used by the Bureau in administering its electronic product radiation control program. However, in order to facilitate this effort, the Bureau also has the authority to require manufacturers of electronic products to maintain testing and distribution records, submit various reports, and, if good cause is shown, permit inspections of their manufacturing facilities. The detailed regulations for implementing the Act and all performance standards established under it are published in Title 21, Chapter I, Subchapter J of the Code of Federal Regulations.

DEFECT AND NONCOMPLIANCE

The FDA Bureau of Radiological Health conducts a program of electronic product regulatory enforcement for the purpose of assuring that all radiation safety defects and failures to comply with standards are adequately corrected. The defect provisions of the law governs all products for which there are no regulatory performance standards. A defect is considered any failure of a product to meet its radiation safety design specifications, or the emission of radiation which creates a risk of radiation injury unnecessary to accomplish the intended purpose of the product. This program includes identification and verification of product defects; close review of a manufacturer's notification of defect; evaluation of the seriousness of each situation; formulation of a practical solution or corrective action to be initiated; and the supervision of implementation of the corrective action program by the manufacturer to its completion.

The following sequence of events has normally occurred in enforcement compliance actions taken by the Bureau. After the Bureau and manufacturer have both become aware of the suspected defect or failure to comply with a standard, the manufacturer is provided with an opportunity to substantiate that no defect or failure to comply exists or that it presents no significant risk of injury. Where corrective action is required, the manufacturer is required to present its proposed plan to the Bureau along with any correspondence which he intends to send to users, dealers, distributors, and others notifying them of the problem and correction program. In addition, the manufacturer must fully describe this scope of the product defect problem including numbers of units involved and their location.

The correction plan and accompanying correspondence are reviewed by the Bureau in light of the intent of the Act and regulations. When the Bureau is assured that the corrective action will satisfactorily eliminate the defect or failure to comply, the manufacturer is permitted to commence implementation of his plan. Corrective action plans that have been approved by BRH are usually implemented in one of the following manners:

(1) Corrections are made to products indirectly by the manufacturer's representatives.

(2) Dealers and distributors are instructed in proper correction procedures and requested to perform necessary repair or modification. All costs are borne by the original manufacturer.

(3) Modification kits designed to correct the defect are transmitted to users for direct and simple application to the product.

(4) If repair is not possible or feasible, the product must be replaced or a cost refund to the consumer can be required.

Throughout the correction program, the Bureau monitors the progress of the corrective action program. After the manufacturer has notified the Bureau that the corrections have all been completed, an audit check of a sample of the products is arranged by FDA to verify that the program has been satisfactorily performed. If, on the basis of this effectiveness check, it is determined that the corrective actions have been adequately completed, the compliance case is then closed.

DEVELOPMENT OF PERFORMANCE STANDARDS

The second principal regulatory authority under the Radiation Control Act requires the Bureau to establish radiation safety performance standards.

Performance standards may be prescribed for electronic products if the Secretary of HEW determines that such standards are necessary for the protection of the public health and safety. The standard may include a definition of the maximum level of radiation emission permissible from an electronic product and may include provisions for the testing of the product and the measurement of their electronic product radiation emissions.

It may also require the attachment of warning signs and labels and the requirement for the provisions of instructions for the installation, operation, and use of such a product.

The Bureau determines the need for a performance standard from many factors, including the results of biological effects investigations, product studies, and reports of potential or demonstrated hazards associated with a type of radiation or a specific product. When the problem area is identified, the Bureau issues a Notice of Intent in the Federal Register announcing its plans to proceed with the development of a standard and requesting all interested parties to comment. Laboratory studies are required from both the engineering and bioeffects viewpoints to develop specialized professional expertise in the area. These studies provide the Bureau with the capability to understand a product and the radiation it emits and to develop a standard that is reasonable, technically feasible and enforceable.

Considerations are given to the latest available scientific and medical data; to the standards currently recommended by other Federal agencies or public or private groups having an expertise in the particular field of electronic product radiation; to the adaptability of standards to the need for uniformity and reliability of testing and measuring procedures; and in the case of components or accessories, the performance of this article when it is assembled in a completed product.

Although there are many reasonable voluntary standards that could be adopted, the law requires BRH to also state the methodology of determining compliance with a regulatory standard. Generally, voluntary radiation standards do not state methods of determining compliance with the standard. Thus, the BRH has had to invest quite heavily in developing new measurement techniques and criteria which were unavailable prior to the passage of the Act.

Early in the development of a BRH performance standard, there is prepared a rationale document which reflects the need for the standard, from the standpoint of engineering and bioeffects considerations, and the basic concepts for assuring radiation safety. This document is progressively expanded in conjunction with the development of the standard to include the scientific and technical basis and other criteria in support of the requirements proposed in the draft standard. When the standard has been developed to a point where it is both useful and technically feasible and its provisions are definitive, a draft Federal performance standard is prepared. This draft standard includes all definitions, performance provisions, emission limits, other required electrical or mechanical safety provisions, and the test procedures that are to be a part of the final standard.

Section 358(f)(1)(A) of the Act provides that the Secretary of HEW must consult a Technical Electronic Product Radiation Safety Standards Committee (TEPRSSC) which represents the public and private sectors concerned with the technical aspects of electronic product radiation safety. This committee is consulted prior to the promulgation of a standard at one or more of its meetings. After a review of the draft standard within TEPRSSC and upon receipt of their advice, the proposed performance standard is published for comment in the Federal Register. It should be emphasized that prior to this publication of the performance standard for official comment, consultations with concerned individuals and organizations have been solicited through every possible channel. Every written comment or record of meetings with industry is retained in a public file which is included in the documentary record of the standard. Publication of the proposed standard in the Federal Register provides an opportunity for additional comment, and these comments and criticisms are carefully analyzed for validity and, where appropriate, changes are made in the proposed standard. A public record is maintained of the analysis and action in response to these comments.

In summary, the chain of events for the development of a standard includes identification of a radiation safety concern, delineation of the need for a standard through bioeffect, product, and other laboratory evaluations; studies of impact and technical feasibility; preparation of a "concept" document; preparation of a draft standard, including significant associated test procedures and laboratory capabilities; review by a statutory committee (TEPRSSC); and publication of the standard for comment in the Federal Register. All of these events occur in the open forum with user and manufacturers cognizance. Appeal procedures providing for remedy are available for protection of adversely affected persons.

FDA PERFORMANCE STANDARD FOR DIAGNOSTIC X-RAY EQUIPMENT

INTRODUCTION

The X-ray Standard, as all standards developed under the authority of P.L. 90-602, is primarily directed to the manufacturer of the equipment and does not directly address nor attempt to regulate the user. It does, however, provide a service to the user by making available x-ray equipment that is certified by the manufacturer to meet specified safety requirements. In addition, the Standard requires the manufacturer to provide to the user, maintenance schedules adequate to keep the equipment in compliance. The user has the obligation to assure that maintenance is carried out although he is not required to do so by Federal law.

The requirements contained in the standard were developed in consultation with manufacturers of x-ray components, assemblers of x-ray systems, user groups, and radiation protection specialists of other governmental agencies. Careful consideration was given to currently recognized National and International radiation protection guidelines, as well as State Regulations, and to the latest available scientific and medical data with respect to ionizing radiation.

Public Law 90-602 requires that its standards be performance rather than design oriented. This is the major reason which precluded the blanket adoption of existing recommendations of groups such as the Council of State Governments, NCRP or ICRP. However, the Bureau did, wherever appropriate, adopt the essential theme covered by such guides and, in addition, incorporated certain new aspects that have been shown to be necessary and technically feasible.

The diagnostic x-ray system is quite different from other electronic products which the Bureau has regulated to date. What is commonly referred to as an "X-ray Machine" has been treated in the standard as a combination of separately manufactured components which are assembled into an integrated system. The nature of this x-ray system and of its manufacture presents somewhat of a unique situation. Because of the variety of components which may be selected for the assembly of a system, the practice of combining components from more than one manufacturer, and the influence of these components on the radiation properties of the total system, we have found it necessary to establish requirements applicable to the individual components as well as to the complete system. Accordingly the standard imposes specific responsibilities on any person engaged in the business of manufacturing major components of an x-ray system (the party commonly referred to as the factory-based manufacturer). Also, it establishes certain requirements for any person engaged in the business of assembling specified components to form an x-ray system or replacing or installing such components in an existing system (the party commonly referred to as the assembler-manufacturer or assembler).

COLLIMATION

One of the most important provisions for achieving a reduction in unnecessary x-ray exposure is the requirement for proper collimation. The standard requires that stationary general purpose radiographic equipment, the equipment that constitutes the largest source of diagnostic exposure to the public, shall be equipped with means for positive beam limitation

(PBL), that is, means to insure the use of x-ray field no larger than the image receptor. The term "image receptor" is used to denote the film, fluorescent screen, or other imaging device that may be used. The positive beam limitation requirement can be met in one of two ways: (1) by providing automatic adjustment of the x-ray field to that of the image receptor size; or (2) by a manually interlocking system which will prevent the production of x-rays until the beam limiting device has been adjusted by the operator to correspond to a size no greater than that of the image receptor.

REPRODUCIBILITY AND LINEARITY

A second area covered by the standard includes two requirements directed toward achieving consistent radiation output. First, with respect to exposure reproducibility, the standard requires that for a specific combination of tube current, tube potential, and exposure time, the variation in measured radiation output based on 10 consecutive radiation exposures taken within a time period of one hour, shall have a coefficient of variation no greater than 5%. Stated another way, a system meeting this requirement will produce exposures such that 95% of them will be within ± 10% of their mean.

The second requirement intended to achieve consistent output is that of "linearity." This addresses the repeatability in exposure output for different combinations of current and time that should result in equivalent exposure output.

The values suggested in the standard for both of these requirements were derived from an analysis of data obtained on old and new equipment by the Bureau and by data requested from industry. The requirements were shown to be technically feasible for good equipment of modern design. Generators meeting these performance criteria provide the user the capability to develop and use exposure techniques that consistently result in diagnostic radiographs with the minimum necessary x-ray exposure.

MISCELLANEOUS REQUIREMENTS

Other requirements in the standard include both audible and visible exposure indicators. With the advent of the SCR solid state exposure switch contactors, it is sometimes difficult to know whether or not an exposure has taken place or is in fact in process since there is no longer the sound of the relays dropping in and out. This could lead to double exposed, partially exposed, or non-exposed films. An adequate signal upon completion of the exposure is an aid to the technologist. It enables him to release the exposure switch as soon as possible after the exposure which will help to lower the heat input into the tube from unnecessary filament boost time. Another item in the standard specifies a back-up timer be provided for systems that are automatic or phototimed with a maximum setting equivalent of 600 mAs for general radiography and 2000 mAs for radiography below 50 kVp.

In addition, the standard requires a visible signal in case the back-up timer terminates the exposure. Before exposures can be resumed a manual reset will have to be accomplished by the operator at the main control panel. The purpose of this is to preclude a series of retakes due to autoexposure timer failure.

Another requirement is for positive filter interlock. This is primarily needed in those situations where varying amounts of filtration are being used with a given piece of equipment. An example of such equipment would be a unit used for general purpose x-ray as well as for mammography. If the unit is being used with 0.5 mm Al for mammography and the tube potential is raised above 50 kVp for general radiographic use, the unit must be locked out until the appropriate filter is in place. In those cases where there is no need to vary the amount of filtration positive filter interlock may be accomplished by merely installing the filter permanently.

As in certain other national and international radiation protection recommendations, the Federal Performance Standard also limits the leakage radiation from tube housing assemblies and beam-limiting devices, controls the amount of filtration in the useful beam, specifies tabletop thicknesses, and specifies the distances from the source to the end of radiographic collimators and to the panel tops of fluoroscopic units.

In all, there are over 60 individual requirements pertaining to all types of diagnostic x-ray equipment including intraoral, radiographic and fluoroscopic units. It is quite detailed and comprehensive. In fact, several people have commented that its great detail may tend to stifle innovation. However, we feel this is not the case because of certain variance provisions which have been included in the regulations to avoid this problem.

VARIANCE PROVISIONS

The x-ray standard is applicable to all diagnostic x-ray equipment which includes a great diversity of types and uses. It was recognized that this diversity could create a problem with regard to the development of a standard that will fully control this product yet not inhibit the development of new equipment and techniques. To handle this problem, regulations were promulgated for the issuance of variances from the standard. A manufacturer will be granted a variance applicable to a total diagnostic x-ray system or a major component if appropriate criteria are met.

A variance may be granted when it is determined that the variance is so limited in its applicability as not to justify an amendment to the standard, or is of such need as not to allow sufficient time for the processing of an amendment to the standard. In addition, the issuance of the variance is based upon a determination that the product: (1) utilizes alternate means for providing radiation safety or protection equal to or greater than that provided by products meeting all requirements of the applicable standard, or (2) utilizes suitable means for providing radiation safety or protection and is required to perform a necessary function or is intended for a special purpose which cannot be performed or accomplished with equipment meeting all requirements of the applicable standard, or for which one or more requirements of the applicable standard would not be appropriate.

COMPLIANCE MONITORING PROCEDURES AND RESULTS

INTRODUCTION

The primary aspects of enforcement of the Diagnostic X-ray Standard include review of manufacturers' reports of their quality control and testing programs, factory inspection, laboratory performance testing, and field performance testing at user facilities.

REPORTS REVIEW

One of the first steps in the enforcement of the standard is the review of the required manufacturers' reports (initial, annual and model change reports) by the Division of Compliance Staff in Rockville, Maryland. The initial reports cover, in detail, the testing and quality control procedures used by manufacturers to ensure that each component meets the standard. Where there is evidence of inadequate testing or poor quality control, the program may be disapproved by the Bureau and if this occurs the manufacturer may not certify his product and thus may not enter it into commerce. As of April 1978, the Bureau has received approximately 3000 reports from 158 manufacturers. Of these, about 1450 have been reviewed and subsequently 30 manufacturer's testing and quality control programs were disapproved (these disapprovals were rescinded following corrections). In addition, 22 separate product recalls were initiated as a result of noncompliant products being discovered through report review. Assember's reports on the installation of certified components are required as a certification mechanism for the assemblers. These provide information on the location and types of certified components that have been installed. Inspections of installed field equipment are then scheduled.

As of May 1978, we have received 50,000 assemblers' reports for new certified systems. An additional 40,000 assemblers' reports for certified components installed into existing systems were received.

PLANT INSPECTIONS

After a manufacturer's testing program has been reviewed, it is necessary to visit the plant. During these visits, the quality control and testing program is observed, samples may be randomly selected for compliance testing, instrument calibration programs are reviewed, and required records are inspected. Manufacturers are visited every one to three years depending on the complexity of their product. Six separate product recalls were initiated as a result of noncompliant products being discovered during plant inspections. We believe a large number of recalls have been prevented by the technical information exchanged between the agency and manufacturers during report review and plant inspections. Since the standard became applicable in August 1974, the FDA has performed 194 inspections of factory-based manufacturers, both domestic and overseas.

LABORATORY TESTING

Laboratory testing is performed on equipment that is small and easily shipped and assembled. Samples of equipment and components are obtained randomly from manufacturers for testing in FDA's Engineering and Analytical Center in Winchester (WEAC), Massachusetts and in Bureau of Radiological Health laboratories in Rockville, Maryland. The testing is conducted with state-of-the-art equipment and techniques. The results accurately reflect the performance of the sample under test.

To date the WEAC laboratory has been conducting compliance testing of only certified dental x-ray equipment, both intra-oral and panoramic. Compatible cephalometric devices are tested in conjunction with intra-oral units. Testing of mobile and portable diagnostic x-ray equipment at WEAC has been initiated.

Practically all requirements of the Diagnostic X-ray Standard are tested for compliance with both the functional and performance requirements. Functional requirements include signals, labels, and required information to be provided to the user and assembler. Performance requirements include collimation, beam quality, accuracy of tube potential, tube current, and exposure time. A complete listing of the tests is given in Table I. Accuracy of technique factors is tested against the manufacturer's specifications. Such specifications are required to be provided to the user or purchaser, and equipment is required to be in compliance with these stated accuracies.

Table 1

Listing of Compliance Tests performed at WEAC on Certified Dental X-ray Equipment.

Functional

1. User Information
    - a. Rating Charts
    - b. Technique Factor Specifications
    - c. Instructions Concerning Radiological Safety Procedures, and Precautions
    - d. Maintenance Schedule

Performance

1. Technique Factory Accuracy
    - a. Peak Tube Potential, Tube Current, Exposure Time (must meet manufacturer's own accuracy specification)

2. Assembler Information
    a. Complete and Accurate Installation Instructions
    b. Compatibility Specifications

3. Signals and Labels
    a. Audible and Visible Signals Indicating X-ray Production
    b. Proper Certification Label
    c. Proper Identification Label
    d. Warning Labels
    e. Preindication of Technique Factors

2. X-ray Beam
    a. Field Size
    b. Minimum Source-Skin Distance
    c. Beam Quality
    d. Exposure Reproducibility
    e. Exposure Linearity

To date, 43 tests of dental systems and components from 19 different manufacturers have been completed. The results are summarized in Table II.

Total compliance was found in 5 of the completed tests.

Results of Laboratory Testing of 43 Certified Dental X-ray Systems and Components.

Functional Requirement	Number out of Compliance	Performance Requirement	Number out of Compliance
Labeling	19	Technique Factor Accuracy	19
Assembler Information	6		
User Information	14	Field Size	5
Preindication of Technique Factors	1	Reproducibility	5
		Beam Quality	6
		Linearity	1

Rockville

Testing at the Rockville facility includes measurement of diagnostic source assembly leakage radiation and aluminum equivalence of tabletops and other materials. In addition, special follow-up compliance testing is performed in the Rockville laboratory.

To date, nine diagnostic source assemblies have been tested for leakage radiation. All were in accordance with the Performance Standard.

FIELD TESTING

In most cases it is necessary to perform field testing. X-ray systems are frequently large complex systems assembled on site from numerous components and therefore impractical to sample for laboratory testing. In addition, the assemblers play a large part in the ultimate performance of the equipment. Field testing also permits an evaluation of individual assemblers.

Field testing is conducted on most general types of equipment, and, as further procedures are developed, will be expanded to include all types of equipment that can be practically field tested. Personnel in the field offices of the Food and Drug Administration as well as persons from 22 State and local Radiological Health Programs who have contracted with the FDA perform this testing with our procedures and equipment. Results of these tests are pooled to attempt to identify trends that may indicate a particular model or manufacturer who has a noncompliance problem. When the problem is identified, a nationwide corrective action or recall is initiated.

Test procedures have been developed for four general types of equipment; Intra-oral Dental, Mobile General Purpose, Stationary General Purpose Radiographic, and Fluoroscopic-spot film. While the radiographic and fluoroscopic functions are often combined in a single machine, time constraints may prevent the performance of a survey of both modes of operation on a single visit.

The items tested are illustrated in Table III. Although different beam sizing requirements apply to the various types of equipment, the concepts of the tests are generally similar.

Table III

Listing of Parameters Tested in Routine Surveys to Measure Compliance with 21 CFR 1020.30, 31, and 32

Functional

1. Information Provided to Users
2. Signals and Preindications of Technique Factors
3. Certification, Information, and Warning Labels

Performance

1. Beam Quality
2. Exposure Reproducibility
3. Exposure Linearity
4. Timer Accuracy
5. X-ray/Light Field Alignment
6. Field Size
7. X-ray/Image Receptor Alignment
8. Light Localizer Intensity
9. Entrance Exposure Rates

As of May 30, 1978, data have been taken and entered into our computer on 3410 dental, 1282 mobile, 4244 stationary, and 1223 fluoroscopic-spot film surveys. Overall results are presented in Table IV.

The variations in the "Number Tested" columns reflect incomplete testing due to equipment failure, data that were rejected in the editing phase of automated data processing, and the testing of systems containing some or all noncertified components such that the Standard did not apply to some aspects of performance.

The results provide an indication of overall trends. Further analysis is performed to identify particular manufacturers, models or even assemblers that are creating the problems.

By far the largest industry wide problem area for stationary radiographic equipment is the collimation performance. Further analysis has revealed that of the certified positive beam limitation systems tested, 7.36% were found to be inoperable. Another 15.5% were found to be noncompliant with the requirements for sizing to the undertable image receptor. If other functional requirements are included, such as automatic return to PBL with change in image receptor, allowance for adjustment to smaller field sizes, and x-ray lockout at incorrect SID(s), then a total of 37.4% of those tested were found to be noncompliant with at least one aspect of the standard.

Several areas of noncompliance are reflected in Table IV. X-ray field sizing is a problem in both the fluoroscopic and spot-film modes of operation. The noncompliances in the category of primary barrier transmission are primarily the result of interlock misassemblies resulting in x-ray production when the primary barrier is not in position to intercept the beam. The problems with entrance exposure rate are primarily a result of miscalibration of the x-ray control allowing selection of tube current and exposure time combinations that deliver an exposure rate in excess of that allowed by the standard. Entrance exposure rates as high as 30 R/min have been observed.

As a result of field testing data, FDA field personnel direct assemblers to initiate corrections immediately.

Table IV
RESULTS OF FIELD TESTS OF CERTIFIED DIAGNOSTIC X-RAY EQUIPMENT

	Stationary		Mobile		Dental		Fluoroscopic	
Requirement	Tested	%NC	Tested	%NC	Tested	%NC	Tested	%NC
Beam Quality	3654	2.8	1127	3.2	3057	8.4	933	4.8
Indicated Field Size	3418	9.7	--	--	--	--	--	--
Light/X-ray Field Alignment	3810	0.5	1197	0.9	--	--	--	--
Reproducibility	3787	1.7	1153	2.2	2828	1.5	912	5.9
Linearity	3609	1.8	241	13.6	717	2.6	77	18.1
Light Intensity	3576	6.3	1075	2.6	--	--	--	--
X-ray/IR Alignment	3077	15.2	--	--	--	--	953	39.1
Combined PBL Requirements	3536	37.2	--	--	--	--	--	--
Field Size	--	--	--	--	3242	--	--	--
Minimum SSD	--	--	1188	1.6	3185	0.9	985	7.4
Entrance Exposure Rate	--	--	--	--	--	--	1079	16.6
Primary Barrier Trans	--	--	--	--	--	--	302	17.8

Note:

-- indicates test is not performed

Data as of June 1978

NC means not in compliance with standard

PROBLEM AREAS AND POSSIBLE SOLUTIONS

INTRODUCTION

Although some programs measure their success by the number of compliance cases and products recalled, we would prefer to attain a goal of 100% compliance and zero recalls. Because no manufacturing process is perfect, there will always be mistakes made and recalls initiated. Recalls are extremely costly for the manufacturer and also for the regulatory agency which must approve and monitor correction programs. It is our job to minimize these costs by improving compliance and finding problems quickly.

REPORTS REVIEW

Reviewing manufacturers' quality control and testing program reports can be an efficient method of finding compliance problems and initiating national recalls. This process has resulted in 22 recalls totalling about 3,750 products.

Our major problem here is the sheer number of reports that must be reviewed. The reports review staff is backlogged by about 1,500 reports. On the average a report has been on file with us 14 months before it is reviewed and a declaration of noncompliance issued. Many products could have been introduced into commerce during that time span.

Bureau records show that after a declaration of noncompliance there is frequently a relatively long time period to the completion of the recall or corrective action program. This is due to the time necessary for the manufacturer to design an appropriate correction program and to make corrections in users facilities. This time range averages about 17 months.

One way to reduce this problem would be to increase the reports review staff so that reports could be acted on when they are received. This may not reduce the number of recalls but certainly would reduce the number of products recalled.

In addition the regulations could be changed to require reports be submitted 3 months prior to introduction of the product into commerce. This coupled with additional positions could eliminate almost all recalls due to report review.

PLANT INSPECTIONS

Plant inspections and report reviews are inseparable. Additional positions could be utilized to make plant inspections more efficient and timely. The number of products recalled would be substantially reduced.

LABORATORY TESTING

Although the laboratory testing program is a very thorough method of testing products for compliance, it has the same drawbacks as the record review process. The lag time between when a product is introduced into commerce and when it is laboratory tested and a declared noncompliance averages about 15 months.

This time would be reduced by additional positions for records review. These individuals are mainly responsible for choosing products to be tested from the manufacturers' reports. It would also be useful to expand the facility at WEAC so that more products could be tested at the same time.

FIELD TESTING

Field testing is performed to develop trends in factory noncompliance so that recalls can be initiated and to monitor the work of individual assemblers.

Trends have been developed by field testing but not quickly enough to prevent costly recalls. The total number of field tests have been small compared to the number of products installed (about 15%) and the number of staff at headquarters have been inadequate to efficiently evaluate the test data.

We hope to improve this situation by increasing the number of states under contract to the Bureau to perform field testing. The agency has provided $400,000 for this. However, additional positions at headquarters will be needed to improve present test data review and to handle the increased workload developed by the new contract states.

The noncompliance rate due to the final assembly of x-ray equipment is high and may be attributed to assemblers cutting corners in their final tests or not following manufacturers' instructions. One method of improving this situation would be to require assemblers to perform the FDA compliance test on each assembly and to file these test results with the Agency. This would not require new authority. An amendment to the regulations would be required.

Another method to reduce noncompliance would be to increase the number of injunctions and civil penalties against assemblers found to continually violate the standard. This method would be an administrative burden that would have to be accepted until the compliance picture improved.

RECALL SUMMARY

The following table summarizes diagnostic x-ray machine recalls and the associated time frames between the introduction of a product into commerce and the completion of a recall or corrective action program. The source indicates where the noncompliance or defect was found. The number of recalls column includes both defect and noncompliance cases. Program disapprovals means the agency officially disapproved a testing program thereby preventing x-ray machines from being introduced into commerce. With regard to the time frame columns, it is assumed that the date products are introduced into commerce is the date the agency received the manufacturer's report.

TABLE V

RECALL SUMMARY OF DEFECTIVE AND NONCOMPLIANT DIAGNOSTIC X-RAY MACHINES

SOURCE	NO. OF RECALLS	NO. OF PRODUCTS	NO. OF PROGRAM DISAPPROVALS*	AVERAGE TIME LAPSE IN MONTHS BETWEEN		
				INTRODUCTION INTO COMMERCE AND DECLARATION OF N/C	DECLARATION AND APPROVAL OF CORRECTION PROGRAM	APPROVAL OF CORRECTION PROGRAM A COMPLETION OF REC
Laboratory Test	11	20,281	5	14.7	3.6	17
Report Review or Plant Visit	28	3,747	6	14.1	5.6	7.4
Field Tests	40	30,395	8	11.5	4.9	9.5
Manufacturer self reporting	19	19,552	0	19.9	4.3	18.8

Note

*25 additional testing program disapprovals were declared that did not require a product recall. The disapprovals resulted from report reviews.

Dr. KENNEDY. Thank you.

Mr. ROGERS. Does FDA have any authority, and are you regulating or setting standards for smoke detectors which contain radioactive material?

Dr. KENNEDY. Again, I will ask my colleague to respond to that.

Mr. ROGERS. Certainly.

Mr. VILLFORTH. We do not have authority for setting standards for consumer products, such as smoke detectors, which use radioactive materials. Those products that use radioactive materials, such as americium, are under the control of the Nuclear Regulatory Commission.

In those situations where consumer products like smoke detectors that include radium—and some smoke detectors—are not under the control of any Federal agency and are only controlled by some State health agencies; in such situations, we have been working to develop guidelines for those State health departments so they can better understand whether certain products, say a smoke detector with radium, might need some additional radiation advisory or consultation or whether it should not be introduced in that particular State. We have worked out a program through a cooperative effort with these States.

Mr. ROGERS. Has the Federal Trade Commission been involved, at your suggestion, as to advertising these products containing a radioactive isotope of some type?

Mr. VILLFORTH. No, sir, we have not dealt with that organization. We have, in the past, suggested to the Consumer Product Safety Commission and prepared some material for their consideration for those consumer products which contain radium, like luminous compounds in wristwatches and, of course, smoke detectors, that those products come under some type of regulatory control. We prepared some material for the Consumer Product Safety Commission, but the Commission felt the priority of such products was not high enough and it has not promulgated any regulation.

Mr. ROGERS. What about radar? Do you have any control over radar? Is there any problem with radar?

Mr. VILLFORTH. Radar, of course, is nonionizing radiation which can effect uniquely different biological consequences.

The answer to your question is that although the Radiation Control for Health and Safety Act, by definition, would allow one to set standards for the radar equipment itself; the generally acknowledged problems of these types of products lie in the exposure or the potential for exposure into the environment. That can be many miles removed from the equipment itself.

Perhaps the article in the recent issue of Newsweek magazine amplifying Paul Brodeur's book on "The Zapping of America" best illustrates the concern of the public and the concern of some critics that there is a proliferation of electromagnetic smog which we are all being bathed in.

There is a genuine concern that the exposure levels to the public from these products, and particularly the multiplicity of these products, needs to be addressed.

Mr. ROGERS. What about computers? Is there any problem with any radiation from computers?

Mr. VILLFORTH. I am not aware of any problems.

Mr. **Rogers**. Has it been checked?

Mr. **Villforth**. I really, sir, would not know quite where to check and wouldn't quite know where the problem would be.

Now, there have been some concerns expressed with the terminals, the display screens. Because those display screens work on the same principles as a television receiver, they have the same potential for problems. But I am not sure I would know where to begin to look into computers. I don't think the voltages are that high. I don't think there would be any exposure potential there. Vacuum tubes of computers are disappearing, so that the potential exposure from such tubes is small. I would guess it would be a nonproblem.

Mr. **Rogers**. You think there is no problem there with the screens?

Mr. **Villforth**. We have looked at the screens. The National Institute for Occupational Safety and Health has looked at screens in some areas, such as the newsroom environment where you have batteries of compositors and others who are working around the clock with these screens, and have found no exposure.

Mr. **Rogers**. What about laser beams?

Mr. **Villforth**. We have a responsibility; we have a regulatory performance standard for lasers, yes, sir.

Mr. **Rogers**. What action has been taken?

Mr. **Villforth**. The standard is in effect and we have taken compliance action against some laser products.

Mr. **Rogers**. I see they are even being used now in discos. Is there a problem there?

Mr. **Villforth**. The problem is whenever one runs into—I am smiling, sir, because this is a very current problem with us; the proliferation of the use of lasers, the nonserious use of lasers, in art forms, as in discos, or the use of lasers out in the Mall in front of the Smithsonian Institution's Air and Space Museum. I would like to say that such use of lasers as an art form as in Wolf Trap this past Saturday night has caused our Division of Compliance considerable consternation. We have defined the groups, the rock groups, the show, the Massachusetts Institute of Technology, who put on the show in the Mall, as manufacturers under a broad extension of the same rationale we use for assemblers.

Therefore, these groups must submit the same type of initial report and be under the same regulatory control as the factory-based manufacturer.

The problem is this is such a new decision and a new approach and the proliferation of disco and art forms is such that we are having a difficult time getting on top of the problem.

Mr. **Rogers**. Is there a problem?

Mr. **Villforth**. The potential is there for some of the larger lasers, which are used in art forms, if the beam strikes people in the audience. And the problem is burns of the eye; damage to the retina from the high energy of the beam hitting the eye, impacting on the retina and causing retinal burn.

Mr. **Rogers**. Could this happen in a disco?

Mr. **Villforth**. It could happen in a disco. It could happen at Wolf Trap, it could happen in the Mall; in a variety of places.

Mr. ROGERS. In other words, if that beam hits the eye of the person, it could cause damage?

Mr. VILLFORTH. If the beam is of a high enough power of a certain type laser, unquestionably, yes. Our job has been to try to set the necessary controls.

Mr. ROGERS. At what level does it become dangerous?

Mr. VILLFORTH. We have in our regulatory performance standard categorized laser power levels simply as level 1, 2, 3, 4. The higher the number, the more the hazard. You start getting skin burns and eye burns at level 4. Level 1 is the lowest level, and it would require an extensive viewing of the laser beam, which is almost an unlikely situation, of getting an exposure.

You find level 3, class 3 lasers are being used by rock groups. The question is, whether there are enough mechanisms built in, interlocks; whether there are enough controls to prevent the beam from bouncing off of a mirror in the back of the auditorium. Are there enough controls to prevent the laser, as it sweeps across the stage, from striking someone in the eye.

Mr. ROGERS. I think if you would give us a broader explanation for the record—not now.

[The following information was received for the record:]

SUMMARY OF PROBLEMS RELATED TO LASERS AND "NON-SERIOUS" USE OF LASER DEVICES

The FDA has been concerned about the growing use of high powered lasers by rock groups and discotheque operators. High powered lasers are also being used to create visual effects in theaters and planetariums and in the advertising industry. Demonstration laser products, including those for artistic purposes and entertainment, are required by the Agency's laser product performance standard (issued in 1976) to meet the accessible emission limits and requirements for class I or class II laser products.

It is difficult to create brilliant visual effects in large areas with class I or class II lasers, and hence many producers of laser light shows have been using class III or even class IV systems. The emissions from a class III laser product pose a definite hazard that is associated primarily with the direct beam. Emissions from a class IV laser product pose even a greater hazard to the eye and the unprotected skin from both the direct beam and its reflections. It is therefore important that exposure to these beams be avoided.

In an effort to clarify the applicability of the standard to laser light shows, the FDA in November 1977 issued compliance guidance which stated that persons who assemble these shows for compensation are considered manufacturers of laser products, and as such are required to assure that their products comply with the standard. The guidance further stated that laser light shows and displays that cannot comply with the standard's requirements for demonstration lasers because they are class III or class IV systems cannot be introduced into commerce unless a variance (a specific authorization to deviate from the standard) has been obtained..

Because processing a variance application or promulgating an amendment to the standard is a lengthy process, the FDA established an interim enforcement policy in February 1978, which specified specific guidelines for safe operation of laser light shows or displays which, if followed, would obviate the need for enforcement action against the laser light show manufacturer. The Agency has given a high priority to inspection of light shows to ensure their compliance to these guidelines.

Other actions that the FDA is taking in this area include the following:

a. Close cooperation is being maintained with State radiation control agencies. As an example, a video tape describing the problems and the Bureau's activities has been made available through the National Radiation Control Television Network.

b. Draft Suggested State Regulations for lasers, including laser light show safety criteria, have been developed in cooperation with the Conference of Radiation Control Program Directors, and

b. circulated for comment to all interested parties. These draft regulations have generated considerable interest, and when developed in final will provide a useful guide for the adoption by each State.

c. The Agency is developing educational materials to be circulated to trade magazines, assemblers, managers and owners of exhibition halls, and other persons to advise them of the potential hazards and what steps the FDA is taking to control this situation.

d. The FDA is cooperating with the Society of Photo-Optical Instrumentation Engineers in seminars on the laser standard, which includes a session on laser light show safety criteria.

Regarding the problems that the Agency is experiencing in laser light shows, they are as follows:

1. The number of laser light shows has increased dramatically in recent years, and there are too many to deal with without an increase in staff to support this program.

2. There are many nontechnical people involved in the management and operation of laser light shows that have no conception of the potential hazards associated with lasers and what it means to comply with the performance standard. This makes enforcement difficult and time consuming.

3. The manufacturers of high power lasers have no restrictions regarding who they sell lasers to, and thus anyone with any degree of knowledge or experience with lasers can purchase these hazardous products.

4. Safety cannot be completely built into the equipment alone, and thus the person who sets up the laser light show and operates it has a major role to play in its safe operation. Thus, with even further amendments to the performance standard regarding the products's manufacturer may not result in increase public safety and would not be addressing the source of the possible problems.

Mr. **Rogers**. Have you contacted State and local health authorities and advised them of this and your standards?

Mr. **Villforth**. We are working very closely with State and local health authorities on this. As the people in our division of Compliance and the field of the Food and Drug Administration get out and visit—for example, there is a group that is now in Johnstown, Pa., looking at the Blue Oyster Cult rock group which was in Baltimore at the Civic Center in March. We have had some problems with them. They have a new type of laser, and wish to introduce a new effect. They will eventually be down here. So we hope to effectively control the use of that laser.

The State people go along with us on these visits. It is a learning experience for them and us, and certainly for the rock groups. Thus, we have to make sure that the public's health is not compromised.

Mr. **Rogers**. What have you done to check your TV situation lately?

Mr. **Villforth**. The TV situation, is similar to the X-ray situation in terms of the levels of inspection. We review reports; we visit manufacturers; we inspect sets in our laboratory to evaluate them in more detail.

Mr. **Rogers**. Have you found any lately that have been emitting any radiation?

Mr. **Villforth**. No. Some of the reasons for this are the changes in technology. Some of the problems we had in 1968 were attributed to certain kinds of tubes—the voltage regulator tubes and some of the circuitry of the set; there have been changes in the state-of-the-art such that these have been designed out of the circuitry and no longer pose a public health problem.

We still have the potential of radiation being emitted off the front of the picture tube which was there in 1968, but the changes in the circuitry are such I think we are satisfied from ones we have looked at, from initial reports, there has been a significant change in the TV situation.

Mr. **Rogers**. But you are still checking?

Mr. **Villforth**. Absolutely.

Mr. **Rogers**. Are the manufacturers still putting on the certificates we required, as I recall?

Mr. **Villforth**. If they don't put on a certificate, they can't introduce into interstate commerce.

Mr. **Rogers**. Have there been any recalls?

Mr. **Villforth**. Perhaps there have been recalls for noncertification.

Mr. **Rogers**. But not from radiation problems?

Mr. **Villforth**. Not recently, no.

Mr. **Carter**. Mr. Chairman.

Mr. **Rogers**. Yes.

Mr. **Carter**. Over the years we have used different methods of delivering radiation. At first we always think that it is extremely good and that it is going to be a cure-all for everyone.

For example, since 1942, 600,000 patients have received radioactive iodine therapy for hyperthyroidism. Do we have any records to show what has happened to these people who have received this therapy? Have they developed cancer, leukemia or other health problems?

Mr. VILLFORTH. We have the thyrotoxicosis study, which was started some years ago, which looked at the population of people who were given these large doses of iodine-131 for therapeutic purposes. The purpose was to follow this population to see if there was a possible incidence of leukemia, and the answer was no; that there was not.

The problem was that the project was terminated, and I can't remember the date. It is in the material we have submitted for the record. The problem was that we didn't look at them long enough to see the possible latent effects of leukemia that might be appearing, say, 20 years later.

We are reexamining that population base.

Mr. CARTER. Did you stop that study, too?

Mr. VILLFORTH. We are starting up that study again.

Mr. CARTER. What date was that?

Mr. VILLFORTH. The thyrotoxicosis study started, I think, in 1961.

Mr. CARTER. With the use of radio——

Mr. VILLFORTH. We are looking at patients administered in 1946 up to——

Mr. CARTER. What years did you say?

Mr. VILLFORTH. We are following patients who, I recall, were administered radioiodine for therapeutic purposes from 1946.

Mr. CARTER. 1942?

Mr. VILLFORTH. It was 1942.

Mr. CARTER. Yes, sir. I am glad that you are doing that. Certainly I would like to see the results of the previous study.

When did this study start? When was it first funded?

Mr. VILLFORTH. Again, I would have to look in the material.

Mr. CARTER. Do you have any preliminary results?

Mr. VILLFORTH. The original thyrotoxicosis study was basically negative. It didn't show anything.

Mr. CARTER. Do you know when this study was started, when it was stopped, and how long it took?

Mr. VILLFORTH. I can look it up here.

Mr. CARTER. You can include that for the record?

[The following information was received for the record:]

RESULTS OF THE ORIGINAL THYROTOXICOSIS STUDY AND THE NEW EXTENSION

The Cooperative Thyrotoxicosis Therapy Follow-Up Study was initiated by the Bureau of Radiological Health, then the National Center for Radiological Health, in 1961 following several years of planning. The objective of the study was to determine whether the incidence of leukemia was increased in hyperthyroid patients treated with I-131, compared to that in hyperthyroid patients treated with other means. The study involved the follow-up of over 36,000 patients treated at 26 medical centers in the United States and Great Britain. The role of the Bureau was to coordinate both the design and data collection phases of the study and to analyze the data once they were collected.

At the end of June 1968, after an average follow-up of approximately 8 years for the 131-treated group, no difference was observed in the incidence of leukemia or thyroid cancer between the groups of patients treated with I-131 or surgery. Data collection was stopped at this time because it was felt that, based on knowledge at that time, the peak period for radiation-induced leukemia had passed. This decision was based on the results from the studies of the atomic bomb survivors in Japan and patients treated with radiotherapy for ankylosing spondylitis, the two large studies which had demonstrated increased leukemia rates associated with radiation exposure. The peak period in these studies for radiation-induced leukemia was about 5 years after exposure. Furthermore, the probability was very small that the difference between the I-131 and surgical groups would become significant. In addition, continuation of data collection would have been very expensive (it had already cost over $6,000,000) and this money was needed in other programs. Therefore, the reasons for terminating data collection in 1968 were both scientific and practical. However, the Bureau did make provisions for centralized storage of all the records from this study on the basis that we might want to re-activate it at a later date.

Subsequently, meetings were held with a number of participating physicians to explore ways of continuing analysis of the study data and publishing other findings of interest. With the passage of time and the knowledge that whole body doses were in the range of interest for the study of low level effects, efforts have been made to obtain further funding from other agencies in order to resurvey the study population. To this end, we initiated in 1977 a resurvey of 3,000 patients at one of the original participating institutions, the Mayo Clinic, to determine morbidity from a mailed questionnaire and mortality in this group after and additional 10 years of observation. This is considered to be a pilot effort to determine if effects are detectable at this time.

Mr. VILLFORTH. It is in the record, sir. It is in that list of material on bioeffects.

Mr. CARTER. Now, I'd like to ask a question about radiation treatment. When an average injection of radioactive iodine is given to a patient with thyrotoxicosis, how many rads are actually delivered to that patient?

Mr. VILLFORTH. It is my understanding around 5,000 to 10,000 rads.

Mr. CARTER. 10,000 rads?

Mr. VILLFORTH. Around 5,000 to 10,000 rads to the thyroid. Rad, r-a-d, not millirads.

Mr. CARTER. To the whole body?

Mr. VILLFORTH. No; I am talking abouth to the thyroid.

Mr. CARTER. I know you are. I would like to have that figure extrapolated to see what the exposure would be to the whole body. If it is 10,000 rads to the thyroid, what is the exposure to the body as a whole?

Mr. VILLFORTH. I can look that up. I don't have it.

The concern we have—and this is in line with your earlier question—of the use of iodine-123 as a potential substitute for iodine-131, is if we can reduce the dose by a factor of 10 with the use of iodine-123, even if there have not been demonstrated a lot of cancers of the thyroid from the use of iodine-131, we still ought to and want to encourage the profession to use the lowest practicable technique, whether it is technetium-99 as a substitute for iodine-131, which can be done in some cases, or iodine-123.

You said something earlier. I would like to amplify on it, if I may, Dr. Carter. That is the concern over the iodine-131, diagnostic levels of iodine-131. We are collaborating to look at another population of people who are administered diagnostic levels of iodine-131. This is a project that is cosponsored by the National Cancer Institute, cofunded by the National Cancer Institute and the Nuclear Regulatory Commission, because both agencies have a mutual concern over the exposure to the thyroid.

Mr. CARTER. I congratulate you. We started out using it in 1942 and now we are trying to find out what it is doing to us. At least you are aware of its dangers. This is one of the things we thought of as a cure-all, a great miracle method of diagnosing and treating diseases.

I have one other question, Mr. Chairman.

In 1961, you began a study on radiologists which you say was not long enough. You have received no answers; is that correct?

Mr. VILLFORTH. You are asking——

Mr. CARTER. I am referring to your study on radiologists and the likelihood of their getting cancer or leukemia.

Mr. VILLFORTH. We have not been as fast as we should have been in the analysis of data.

Mr. CARTER. Yes, sir; but you are no longer funding that study, are you? I believe you said you stopped funding it, did you not?

Mr. VILLFORTH. That's correct; the data collection phase of the study has been terminated.

Mr. CARTER. How are you ever going to find out the long-term effects if you stopped funding it?

Mr. KENNEDY. I think there may be some confusion here, Dr. Carter. May I try to explain?

We have been contracting outside the Agency for the data-gathering part of the study, and we are now doing the analysis inhouse. We did terminate the outside data-gathering contracts. So, in essence the study is still going.

It is just that we are paying for it in FDA salaries instead of outside contracts to gather the data.

Mr. CARTER. When did you stop your outside contracts?

Mr. KENNEDY. What was the date? Two years ago, I believe; 1976.

Mr. CARTER. Two years ago. And after 2 years of an analysis, you have reached one conclusion and that is——

Mr. KENNEDY. No, no, Dr. Carter, that was the only conclusion, the only positive conclusion that emerged from the 1961 study, not from this study.

From this study, the newer sample, we are continuing the analysis and will get back to you about what we find, but it is not complete. I do not think we have come up empty on this one. I hope not.

Mr. CARTER. Thank you very kindly.

Thank you, Mr. Chairman.

Mr. ROGERS. Let me quickly go into some questions, if I may.

We also submitted, I think, some questions to the staff to be answered for the record. How many people are now working in the Bureau of Radiological Health?

Mr. KENNEDY. I think I would like Mr. Villforth to answer that.

Mr. VILLFORTH. I am tempted to say how many people are employed in the Bureau? We have approximately 400 people employed in the Bureau of Radiological Health, and I am satisfied they are all working. There are about 473 person-years in 1978 committed to radiological health efforts; the remaining being done by the field force of FDA, which is not a part of the Bureau of Radiological Health.

Mr. ROGERS. But you actually have 400 people.

Mr. VILLFORTH. About 400 people.

Mr. ROGERS. Not man-years, but people, persons?

Mr. VILLFORTH. Persons, living bodies. Beyond that, we have additional numbers of people working part time and some working full time in the field, and the amounts to a total in FDA about 473 person years for ourselves and the field in radiation.

Mr. ROGERS. How many in the field; actual person in the field?

Mr. VILLFORTH. I can't answer that because it is more than the 73, because some are working part time with us and some are doing medical device inspections. So not all of these people are working full time on radiological health matters. Some are working part time in radiological health and part time on medical device matters.

Mr. KENNEDY. But it is 73 person-years in the field.

Mr. ROGERS. Dr. Carter?

Mr. CARTER. I was just reading a statement here from a medical magazine that said that the occurrence of thyroid tumors is generally between 5 and 30 years after radiation exposure, but that a person may develop thyroid tumors as long as 50 years after radiation.

Thank you, Mr. Chairman.

Mr. **Rogers**. How does your employment figure compare to 1972? Is it more or less?

Mr. **Villforth**. There were less in 1972.

Mr. **Rogers**. How many less, any idea? You don't have to be exact.

Mr. **Villforth**. I would say there are about 50 person-years less.

Mr. **Rogers**. How many people less?

Mr. **Villforth**. I am no sure I can answer that. I have the data.

Mr. **Rogers**. If you will put in the record——

Mr. **Villforth**. We can show you the trends in our person-years.

Mr. **Rogers**. Has it been more or less?

Mr. **Villforth**. It's increased.

Mr. **Rogers**. It is increasing?

Mr. **Villforth**. Yes.

[The following information was received for the record:]

FDA Radiological Health Personnel Trends

Fiscal year:	*Positions*
1972	408
1973	425
1974	436
1975	443
1976	466
1977	474
1978	473

Mr. **Rogers**. What is you budget?

Mr. **Villforth**. The FDA budget for fiscal year 1978 is about $21 million for radiological health.

Mr. **Rogers**. What was it last year?

Mr. **Villforth**. In 1977, it was $19 million. In 1976, it was $17.6 million.

Mr. **Rogers**. So it has been increasing about $2 million?

Mr. **Villforth**. Yes, sir.

Mr. **Rogers**. Do you have a grant and a contract program?

Mr. **Villforth**. Yes, sir.

Mr. **Rogers**. How much intramural research is being done? Any?

Mr. **Villforth**. In the ionizing radiation area?

Mr. **Rogers**. Just lump it all together; first the field and then you can break it down.

Mr. **Villforth**. I don't have it in toto, but let me give you an example of what it would be in the ionizing radiation area.

Mr. **Rogers**. What do you mean you don't have it in toto?

Mr. **Villforth**. I don't have it in front of me. I can get it for you. Let me give you an illustration. In the ionizing radiation area, we have about $360,000 in grants, about $2.9 million in contracts, and about $9.9 million in intramural operations. These funding levels reflect our manpower of approximately 311 man-years, with an average of something like $34,000 per man-year in payroll and other direct operational expenditures. So our total ionizing radiation program for fiscal year 1978, intramural, extramural grants and contracts, is about $12.8 million.

I can give you comparable figures for the total Bureau, which would include other radiations.

Mr. Rogers. Yes; if you would give us a breakdown of all of this, I think, and show a comparison.

[The following information was received for the record:]

FISCAL YEAR 1978—FDA RADIOLOGICAL HEALTH PROGRAM RESOURCES

Program area	Total positions	Total funds (M)	In-house funds (M)[1]	Extramural funds (M)[2]
Ionizing	311	12.8	9.9	2.9
Light	80	3.7	3.2	0.5
Sonic	26	1.2	0.9	0.3
RF/microwave	56	2.5	2.2	0.3
Total	473	20.2	16.2	4.0

[1] Includes personnel and direct operations costs for headquarters and field.

[2] Includes contracts, interagency agreements, and grants for headquarters and fields.

Mr. Rogers. Has your budget for grants and contracts gone up?

Mr. Villforth. The budget, the disposition between grants and contracts and intramural is partly an internal decision as to where we feel——

Mr. Rogers. I understand that.

Has your contract program gone up? Has your grant program gone up? Has your intramural program gone up or down?

Mr. Villforth. The total effort is slightly increased from what it was.

Mr. Rogers. Would you give us the specifics?

Mr. Villforth. Surely.

Mr. Rogers. Are there any areas where it has decreased?

Mr. Villforth. I have, for example, an illustration, graphic illustration of the Bureau's total programs.

Mr. Rogers. I am not asking that. I don't think you understood my question.

I am saying, has your grant program gone down; has your contract program gone down or has your intramural program gone down?

Dr. Kennedy. What were the trends in partitions?

Mr. Rogers. That is what I am trying to say.

Mr. Villforth. Our grant program has gone down.

Mr. Rogers. From what?

Mr. Villforth. In 1972, the grant program was about $2 million.

Mr. Rogers. It is down to $300,000?

Mr. Villforth. In the ionizing radiation area, it is down to about $360,000 all together.

Mr. Rogers. Give us a breakdown of that and where it is going. How many people are covered in your grants; how many people are getting grants out of the $312,000?

Mr. Villforth. I believe there are 20-some grants now.

Mr. Rogers. What are those grants involved with, mainly?

Mr. Villforth. The majority of these are in the nonionizing radiation area.

Mr. Rogers. Doing what?

Mr. Villforth. Either looking at the biological effects of light, ultrasound and, to some extent, microwave RF, or looking at methods of measurement, detecting systems.

Mr. ROGERS. Would you let us have a breakdown of what those are, what results are being shown, how long they have been in existence, the principal investigator and what results are coming about?

Mr. VILLFORTH. Sure.

[Testimony resumes on p. 463.]

[The following information was received for the record:]

SUMMARY OF FDA/BRH
ACTIVE GRANTS

TITLE: Transfer Mechanisms in Irradiated Biological Systems

GRANT NO: FD 00632-12S1

GRANTEE: N.Y. State Dept. of Health
Albany, New York

PRINCIPAL INVESTIGATOR: Harold C. Box

ACTIVE DATE: 6/1/66 - 7/31/78

TOTAL SUPPORT: $276,496

FY 1978 SUPPORT: $17,468

OBJECTIVES: This project is aimed at achieving an understanding of the molecular changes induced in biological systems by ionizing radiation. Working at very low temperatures (4°K or less) primary radiation products are being identified in biological compounds such as peptides and nucleotides. Secondary radiation damage processes, electron transfer, proton transfer and hydrogen abstraction processes can subsequently be followed at higher temperature. The main experimental tool used in the identification of radiation products and processes is electron-nuclear double resonance (ENDOR) spectroscopy.

PROGRESS/SIGNIFICANT RESULTS: The research supported by this grant was a study of radiation effects at the molecular level. With this support a combination of magnetic resonance and cryogenic techniques were developed for stabilizing and identifying the initial chemical products generated by ionizing radiation in biological substances. The most basic accomplishment was the recognition that radiation damage at its most primitive chemical stage can be categorized as arising from either radiation-induced oxidation or reduction. Primitive oxidation and reduction accounted for all of the products in almost all cases with equal amounts arising from oxidation and reduction. An interesting exception, discovered in the last year of the grant, was the case of electrons trapped intermolecularly so that no molecular reduction product was formed. The phenomenon of trapped electrons, which occurs only in the presence of molecules of low electron affinity, provided a unique opportunity for the study of charged particles by polarization effects.

TITLE: Neoplasms in Irradiated Human Populations

GRANT NO: FD 00634-14

GRANTEE: University of Rochester
Rochester, New York

PRINCIPAL INVESTIGATOR: Louis H. Hempelmann

ACTIVE DATE: 1/1/64 - 12/31/79

TOTAL SUPPORT: $815,610

FY 1978 SUPPORT: $36,577

OBJECTIVES: The project is a study of the risks of neoplasms in irradiated human populations with considerable emphasis on people treated with x rays in infancy and on women given x-ray treatments to the breast for post-partum mastitis. The control groups for women given x-ray treatments to the breast have been extended to include non-irradiated siblings and women with acute mastitis at New York Hospital not treated with x rays.

PROGRESS/SIGNIFICANT RESULTS: For 20 years breast cancer has been studied by mail survey in 606 women treated with x rays for acute post-partum mastitis. Three cases of cancer developed in the non-irradiated breasts of 415 women treated unilaterally and 34 in the 797 treated breasts in the total population. The incidence of neoplasms was compared with that of three non-irradiated control groups, namely, non-irradiated sisters of the treated women, women with acute post-partum mastitis not treated with x rays and their non-irradiated sisters. The mean ages of the treated and control groups and follow-up periods were comparable. Except for a higher frequence of chronic cystic mastitis, the risk factors (other than radiation exposure) did not favor the increased incidence of breast cancer found in the irradiated women. The relative risk (RR) of the treated group was 2.0 for cancer and 1.9 for benign neoplasms. A linear dose response was observed using total cumulative doses per patient (to both breasts) and the non-irradiated groups as controls. For comparable total doses, fractionation of exposures (1-2 versus 3-4 treatments) did not reduce carcinogenic action of the x rays. The latent period varied inversely with the total dose with ten years probably representing the minimum latent period. Women over 30 at the time of irradiation had a higher risk of developing breast cancer than younger women. After a 15 year latent period, the RR of the irradiated women was more than three times that in the controls and the RR of irradiated breasts was 4.7 times that of the non-irradiated breasts in women treated unilaterally.

The absolute risk of developing cancer was between seven and ten cases per million women exposed to one rad per year.

In another study, a mail survey of 2,873 persons treated with x rays in infancy for alleged thymic enlargement, the obtained information suggested an increase in the frequency of asthma and of rare illnesses in the irradiated population were twice and three times those in the non-irradiated siblings. Immunologic tests in a small sample of the irradiated population, however, did not reveal evidence of immunologic deficiencies or aberrations.

The study was designed to determine the incidence of radiation induced neoplasms in the irradiated population, but the incidental finding of an increase in rare diseases with immunologic features was unlikely to be explained by chance. Such diseases could be related to radiation damage of the thymus gland in infancy.

TITLE: Studies of Thermoluminescent Dosimeter Systems

GRANT NO: FD 00639-09

GRANTEE: University of Washington
Seattle, Washington

PRINCIPAL INVESTIGATOR: Thomas G. Stoebe

ACTIVE DATE: FD 00639-09

TOTAL SUPPORT: $389,401

FY 1978 SUPPORT: $43,007

OBJECTIVES: The objectives of this research program is to extend the usefulness of thermoluminescent dosimeter systems in the detection of certain nonionizing radiations and to improve this capability for magnesium oxide and lithium fluoride after x-ray, ultraviolet and ultrasonic irradiation, in samples with carefully controlled impurity concentrations and lattice defect structures. The techniques used include thermoluminescence measurements, ionic conduction, crystal deformation, and optical absorption. These studies provide scientific knowledge regarding the relationship between defect-related properties and thermoluminescent processes while supplying the necessary understanding for the development of improved thermoluminescent radiation dosimeters.

PROGRESS/SIGNIFICANT RESULTS: The higher purity materials continue to show the highest TL sensitivity, as evidenced by the results on the high purity Spicer samples. Norton crystals are more readily available commercially, and further TL sensitivity comparisons need to be made between different Norton and Spicer crystals, with a possible correlation being made with impurities responsible for or involved in the TL Process.

The response of Spicer crystals between 230 and 390nm is constant to within a factor of about two. This extends the range of the same observation seen earlier. Sensitization by annealing at 1000°C is effective in increasing TL output by a factor of between 2 and 4; previous work indicated an increase of a factor of 10 caused by annealing at 2000°C. The time decay of the peak is about the same as reported earlier. All of these results indicate the generality of the observations made earlier, although additional samples must be tested to provide further confirmation.

Results obtained on powdered samples and pressed disks were not as promising as expected, since TL outputs in all cases were lower than in the single crystals. However, making single crystals into powders allows one to homogenize the samples relative to impurity content by mixing the powders, pressing and sintering. It is possible that the low sensitivities resulted from interaction with humidity in the case of powders and additionally with the water used to produce the pressed disks. These experiments of making pressed disks are quite new, and results (especially reproducibility) should improve with experience and with slight modifications in procedure.

TITLE: Biopsychological Studies of Microwave Irradiation

GRANT NO: FD 00650-06

GRANTEE: University of Kansas Medical Center
Kansas City, Kansas

PRINCIPAL INVESTIGATOR: Don R. Justesen

ACTIVE DATE: 9/1/76 - 8/31/80

TOTAL SUPPORT: $331,656*

FY 1978 SUPPORT: $81,174

OBJECTIVES: To assess acute and chronic behavioral and biological sequelae of radiation of animals by microwave energy in dose-determinate exposures, i.e., in the multi-mode cavity.

PROGRESS/SIGNIFICANT RESULTS: Preliminary work revealed an inverse monotonic relation between latency of the first prominent peak of the visually evoked electrocortical response (VER) (N_1) and cerebral temperature as elevated in 1.0-°C by a succession of brief exposures to an intense microwave field. When brain temperature during a single intense exposure was elevated briefly to 43°C (more than a few seconds at this high level can be fatal), a curvilinear relation was observed during a series of measurements of the VER as temperatures fell toward basal levels. One gathers from the much longer latencies of VERs that are observed after attainment of a very high temperature that there is a transient but reversible poisoning of the cerebrum if attainment of 43°C does not prove fatal. Twenty-four hours after exposure to the intense radiation, surviving guinea pigs have presented no electroencephalographic evidence of insult and, that in which radiation occurred and that a few meters away in which VERs were measured. Basal rectal temperatures, even after extensive handling and during control sessions, remained very high (39°C) in the guinea pigs.

*Estimated Total Cost

TITLE: Effects of Prenatal . ongitudinal Study

GRANT NO: FD 00654-06

GRANTEE: Johns Hopkins University
Baltimore, Maryland

PRINCIPAL INVESTIGATOR: Mary B. Meyer

ACTIVE DATE: 1/1/72 - 7/31/79

TOTAL SUPPORT: $252,425*

FY 1978 SUPPORT: $44,902

OBJECTIVES: This is a long-term epidemiological study to investigate the possible effects of x-ray exposure during fetal life on subsequent development, health and reproductive experience in females. The study population comprises 1458 females exposed in utero to maternal diagnostic x rays such as pelvimetry.

PROGRESS/SIGNIFICANT RESULTS: Phase I of the study showed a 10-15% increase in fertility in young exposed women, based on ascertainment of live births and fetal deaths registered in Baltimore City. This statistically significant difference ($p = .011$) remained after adjustment for differences between exposed and control women in economic, social and medical factors.

Phase II of the study, a direct follow-up of exposed-control pairs of women now aged 22-28, continues to show more total pregnancies among exposed women. Exposed in-utero women had 15% more total pregnancies than controls in 1960-1969, and 7% more in 1970-1975. Exposed and control women are similar in number of siblings, number of children wanted, contraceptive use, and frequency of therapeutic abortion. Other findings suggest possible exposed-control differences in growth, development, and behavior. Exposed women have completed fewer grades of school, have poorer general health, more menstrual problems, more of certain diseases and accidents, and are heavier for height than controls.

---

*Estimated Total Cost

TITLE: Cell Damage by Near UV Light and Tryptophan Photoproducts

GRANT NO: FD 00658-07

GRANTEE: University of Missouri
Columbia, Missouri

PRINCIPAL INVESTIGATOR: Abraham Eisenstark

ACTIVE DATE: 2/1/76 - 5/31/79

TOTAL SUPPORT: $179,286

FY 1978 SUPPORT: $34,048

OBJECTIVES: Bacterial mutants have been found that are highly sensitive to visible and near-ultraviolet light and to a tryptophan photoproduct (TP). These mutants also lack the ability to undergo genetic recombination (i.e., they are recombinationless mutants). The broad objectives of this research are: (1) to complete the separation and identification of the tryptophan photoproduct that causes these biological damages; (2) to identify the macromolecule with which tryptophan photoproduct interacts (i.e., DNA, one of the repair enzymes, primer RNA, etc.); (3) to determine the specific manner whereby TP interferes with genetic recombination, DNA repair and replication; and, (4) to test the abiotic effects of TP in more complex biological systems.

PROGRESS/SIGNIFICANT RESULTS: Near ultraviolet (NUV) irradiation of tryptophan photoproducts, including H_2O_2, that are selectively toxic to rec mutants of bacteria. These photoproducts inhibit repair of bacterial single strand DNA breaks and replication gap closure. Also, H_2O_2 greatly enhances NUV inactivation of bacteria and phage. In bacteria, two types of synergism are operative: at low H_2O_2 concentrations, increased killing results from inhibition of rec A dependent repair processes; at high concentrations, synergistic killing proceeds independently of the functional state of the rec A gene product. Although killing by H_2O_2 alone can be directly correlated with induction and capacity to repair SS breaks, both genetic and biophysical evidence indicates synergistic killing of T7 by NUV plus H_2O_2 is the result of DNA-protein crosslinks, which prevent DNA injection into host cells. This synergism occurs maximally at 340nm, and may be dependent upon the generation of superoxide anion from the NUV photolysis of H_2O_2. To test mutations by NUV plus H_2O_2, a testing scheme for low dosages with long exposures is being developed. In particular, a modified fluctionation test has been utilized. These results present insights into understanding the complexities of NUV radiation on biological systems, both alone and in concert with H_2O_2.

TITLE: Ultrasonic Toxicity Study

GRANT NO: FD 00665-06

GRANTEE: Indianapolis Center for Advanced Research
Indianapolis, Indiana

PRINCIPAL INVESTIGATOR: Francis J. Fry

ACTIVE DATE: 6/1/73 - 8/31/79

TOTAL SUPPORT: $582,160

FY 1978 SUPPORT: $110,302

OBJECTIVES: Rapid advances in the use of ultrasound as an atraumatic non-invasive diagnostic modality for clinical medicine has focused attention on the need for definitive toxicity information on this energy form to aid in establishing some answers to just how safe is this apparently safe technique. As a significant first step in helping to provide an answer to this highly pertinent question, the reproductive organs and the pregnant uterus and fetuses of the mouse are being irradiated in a manner similar to that used for human clinical diagnostic procedures on these body tissues and systems for which clinical evaluation shows every evidence of apparent safety. By using the experimental animal, the clinical information can be buttressed and upper limits of ultrasonic dosage can be established in a manner not appropriate for the human circumstance.

PROGRESS/SIGNIFICANT RESULTS: Ultrasound in a delivery format similar to that used clinically in pulse echo diagnostic techniques (1 MHz frequency range, 100 Hz pulse repetition frequency) has been applied to the male mouse testicles, non-pregnant female mouse ovaries and pregnant mouse uterus at day 8 of gestation. The time average spatial peak intensity for a 20 second irradiation period at each matrix site for onset of adult mortality in the males and non-pregnant females is essentially 70 watts/cm^2. These data are for a focused beam having a 6 dB beam width of 2 mm. For the pregnant animals, adult mortality begins at 23 watts/cm^2. Significant changes in litter size occur for similar intensity levels. When anomalies which occur in controls are significantly increased for irradiated animals (a striking feature of this study is the almost total lack of appearance of anomalies in irradiated animals which are not present in controls), this increased incidence is not always presented in a unidirectional manner as a function of increasing average intensity. As the average intensity levels are gradedly increased to 180 watts/cm^2 there is generally an increased incidence of a given bioeffect. There are, however, some notable exceptions to this generalization. When a 6 dB beam width of 4 mm is used with the pregnant animals the adult mortality begins at 8 watts/cm^2.

TITLE: Structure of a Cell-Lethal Tryptophan Photoproduct

GRANT NO: FD 00674-05

GRANTEE: University of Missouri
Columbia, Missouri

PRINCIPAL INVESTIGATOR: John P. McCormick

ACTIVE DATE: 3/1/74 - 5/31/81

TOTAL SUPPORT: $128,948

FY 1978 SUPPORT: $32,280

OBJECTIVES: Near-UV (ultraviolet) (300-375 nm) irradiation of oxygenated, aqueous tryptophan solutions gives rise to the mutagenic, cell-lethal agent, hydrogen peroxide, as well as N-formylkynurenine (NFK), and effective, near UV photosensitizer. These two photoproducts then enhance the photodegradation of biological organisms, including bacteria and bacteriophage. It was found that ortho-acetylformanilide (oAF, a close NFK analog) to be an effective, near-UV photosensitizer for necleoside photooxidation and hydrogen peroxide formation. The proposed work will involve identification of the near UV oAF-sensitized oxidation products formed from guanosine, adenosine thymidine, uridine, and cytidine.

The mechanism(s) by which these photosensitized oxidations take place will be investigated. In particular, experiments will be carried out to examine the possible involvement of the superoxide anion and excited state (singlet) oxygen.

Near-UV and hydrogen peroxide effect synergistic killing of both bacteria (Escherichia coli) and bacteriophage (T7). The proposed work will investigate the chemical basis for the molecular changes which are caused by these agents acting in concert, including the possible involvement of the reaction of hydrogen peroxide with superoxide anion to form the highly oxidizing hydroxy radical.

The generality of these processes will be investigated, by further examining what other types of near-UV, biological chromophores can act as photosensitizers, what types of bio-molecules are subject to near-UV photosensitized oxidation and hydrogen peroxide generation, and what types of protection against this photooxidative destruction organisms may possess.

PROGRESS/SIGNIFICANT RESULTS: Identification of the cell-lethal Trp photoproduct - Chromatographic, chemical, and biological characterization led to the identification of H_2O_2 as the only Trp photoproduct which has the observed (vide supra) selective cell toxicity.

Study of the mechanism of H_2O_2 formation - Experiments have revealed that upon near-UV irradiation Trp is rapidly transformed to a significant extent into NFK, which becomes the photosensitizer which mediates H_2O_2 is formed primarily by a pathway involving O_2^-, but a separate pathway involving $^1O_2$ also gives rise to some H_2O_2. In addition, O_2^- has some other fate (s), perhaps leading to NFK formation. The involvement of O_2^- was demonstrated using SOD, which substantially enhanced H_2O_2 formation when present during the photolysis.

Near-UV promoted formation of H_2O_2 from other biomolecules - Irradiation of Guo, Ado, Thd, Urd, or Cyd (or the corresponding 5' monophosphates) with near-UV in the presence of oAF (a close analog of NFK) results in the oxidation of these compounds, with formation of comparable amounts of H_2O_2. This process is strongly pH dependent, with low pH being most favorable for photooxidation. As well, irradiation of His, Tyr, and Met under these same conditions gives rise to H_2O_2; however, when any of eighteen other amino acids are the substrates, H_2O_2 is not formed to any significant extent.

TITLE: Ultrasonic Radiation on Nucleic Acid and Components

GRANT NO: FD 00675-04

GRANTEE: Johns Hopkins University
Baltimore, Maryland

PRINCIPAL INVESTIGATOR: Shih Y. Wang

ACTIVE DATE: 6/24/74 - 11/30/80

TOTAL SUPPORT: $305,010

FY 1978 SUPPORT: $79,648

OBJECTIVES: Nucleic acids play a key role in cellular functions. Because chemical alterations in active nucleic acids by UV-, x-, and Y-ray radiation produce mutagenic, lethal, and other biological effects, ultraviolet and radiation chemistry and biology of nucleic acids have been in the foreground of scientific research for the past three decades. Therefore, in order to understand the action of ultrasound on biological systems, studies on ultrasonic radiation of nucleic acids and their components are essential especially in considering the increasing clinical use of ultrasound. The systematic investigation will continue to be conducted in a dual fashion: (1) the study of the sonochemical change of nucleic acid bases, nucleosides, and nucleotides and polynucleotides at low levels of H. influenzae transforming DNA and of the degradation of SV40, x-174, and T7 DNA. The effects of various parameters such as temperature, concentration, sonic intensity, pH, ionic strength, dissolved inert gases, etc. will be examined. Dose response studies, analyzed by high pressure liquid chromatography for the appearance of sonoproducts, the decrease in the UV absorbancy of the reactant, and, in addition, by radioactivity distributions of labelled compound after sonication and chromatography.

At the same time, the biological studies will emphasize on establishing the threshold conditions of inactivation of transforming DNA and of single and double-strand degradations of superhelical and various DNAs.

PROGRESS/SIGNIFICANT RESULTS: Again this research has been following two directions: (1) the study of the sonochemical changes in nucleic acid components at a low level of sonication (0.5 - 5 W/cm^2, 1 MHz) and the examination of sonophysical effects, i.e., strand breakage in nucleic aciss. By measuring the decrease of their characteristic ultraviolet absorbancies and by analyzing the time-dependent formation of various sonoproducts, several "threshold" intensities have been assayed. They were found to be in the range of 0.5 - 1.0 W/cm^2 depending on experimental conditions. Dose response studies of nucleosides in aqueous solutions indicate that these rates are somewhat slower than those of the corresponding bases. In addition to the sonochemical changes of the base moieties, the cleavage of ribosidic linkages is evident in the sonicated nucleosides. On the other hand, by studying the sedimentation coefficients of sonicated double-stranded T7-DNA and circular SV 40 DNA in sucrose gradients, the lack of chain breakage at a low level of ultrasound has been demonstrated. These results again seem to suggest that chemical modifications occur in DNA prior to the loss of its viability.

TITLE: Ultrasound Effects on Nucleic Acids and Cell Cycle

GRANT NO: FD 00694-05

GRANTEE: University of Rochester
Rochester, New York

PRINCIPAL INVESTIGATOR: Morton W. Miller

ACTIVE DATE: 4/1/74 - 6/30/79

TOTAL SUPPORT: $250,166

FY 1978 SUPPORT: $71,870

OBJECTIVES: Very high frequency sound (ultrasound) has a variety of applications in medical practice. Low intensities are utilized in certain fetal diagnostic situations, moderate intensities for certain types of therapy (heating), and high intensities for certain types of non-invasive surgery. The use of ultrasound in diagnosis and therapy is done with the assumption that it is safe from posing as a potential human health hazard. The objective of the research program is to expose biological material to therapeutic levels of ultrasound and to determine if any biological perturbation results: the biological parameters to be analyzed include growth, cell progression, chromosomal mutagenicity, DNA, RNA and protein syntheses, and DNA molecular weights. If perturbations are found the physical mechanism(s) causing the perturbation will be sought.

PROGRESS/SIGNIFICANT RESULTS: The research results indicate that biomedical ultrasound is capable of inducing perturbations in several plant and animal systems; these perturbations include reduced growth rates, reduced mitotic indices, induced cell wall shattering, induced chromosomal anomalies, reduced macro-molecular synthesis, cell lysis, loss of viability, and induction of giant cells. All of these parameters, with the exception of the cell wall shattering and lysis, generally pertain directly to effects on the genetic and regulatory mechanisms of the cells. What appears evident at this juncture is that biomedical ultrasound is capable of affecting eukaryotic cell progression.

TITLE: Recovery of Human Cells from Ultraviolet Damage

GRANT NO: FD 00755-03S1

GRANTEE: University of Texas at Dallas
Richardson, Texas

PRINCIPAL INVESTIGATOR: Helga B. Harm

ACTIVE DATE: 6/15/75 - 12/31/79

TOTAL SUPPORT: $166,145

FY 1978 SUPPORT: $38,930

OBJECTIVES: Humans are to varying extents exposed to near-ultraviolet radiation from sunlight or technical light sources. The resulting lethal and mutagenic lesions in cellular DNA are mainly cyclobuta-dipyrimidines ("pyrimidine dimers"), which can be removed by dark repair processes or reversed to the corresponding monomers by absorption of slightly greater wavelengths after complexing with photoreactivating enzyme (PRE). Only recently PRE was discovered in cells of higher mammals including man. The objective of these studies is to investigate the recovery effects in UV-damaged cells with emphasis on their photo-repair.

PROGRESS/SIGNIFICANT RESULTS: To induce DNA lesions in cultured mammalian cells, particularly fibroblasts from potoroo cornea, mouse skin (3T3), cat cornea, human skin (healthy and diseased; low and high passage number), and freshly obtained ox cornea tissue, 254-nm radiation or 302-nm radiation (the latter being part of the solar spectrum) was used. White light (WL) from "Daylight" fluorescent lamps was either applied subsequently as photoreactivating light, or as damaging radiation itself. Unirradiated samples under otherwise identical conditions served as controls. DNA from cells treated in these different manners was extracted and tested for its capability of competitively inhibiting photoenzymatic repair of UV-irradiated Haemophilus influenzae transforming DNA in vitro in the presence of PRE from yeast and photoreactivating light.

(1) Illumination with unfiltered WL (which includes wavelengths shorter than 380-nm) occasionally leads to a small photoreactivation effect in UV-irradiated cells. If applied without previous UV-irradiation, it causes by itself damage that results in competitive inhibition of photorepair in the in vitro test system.

(2) The WL damage can be minimized by a combination of several conditions: (a) lowering the temperature during exposure, (b) nitrogen gassing of the cells, and (c) elimination of all wavelengths 380-nm by filtering the light through a plate of suitable plexiglass.

(3) The conditions mentioned under (2) are favorable for observing photorepair, presumably because the latter is not counteracted by adverse effects of the WL itself. Illumination of UV-irradiated cells with filtered WL (essentially 400-nm) results in considerably less competitive inhibition by their DNA in the in vitro test system that if the same UV-irradiated cells were not illuminated. This suggests the occurrence of photorepair. For example: quantitative evaluation of the curves indicates about 90% photorepair of lesions in potoroo cornea cells, and about 70% in two different human cell strains from healthy donors, but at high passage number (the latter seems to be important).

(4) A similar damaging effect to DNA as observed after unfiltered WL illumination is found after hydrogen peroxide treatment of cells in the dark.

(5) The effects mentioned under (1) through (4) seem to apply fairly generally to mammalian cells. Since the potoroo (a marsupial) is known to possess PRE extensive studies with cells of this species served as a guideline for comparative studies with higher mammalian cells.

TITLE: Cumulative Teratogenesis From Low-Level Microwaves

GRANT NO: FD 00790-02

GRANTEE: Washington University
St. Louis, Missouri

PRINCIPAL INVESTIGATOR: Fred J. Rosenbaum

ACTIVE DATE: 5/1/76 - 7/31/78

TOTAL SUPPORT: $96,483

FY 1978 SUPPORT: -0-

OBJECTIVES: Recent work has shown that prolonged exposure to low-level microwave radiation (0.5 mW for 8 hrs. at 9GHz) will induce putatively cumulative teratogenic damage in pupae of the darkling beetle Tenebrio Molitor. The work proposed is to determine: (a) whether intermittent exposure to microwave energy during pupation causes like damage, as predicted by previous results; (b) the power level for putatively thermally induced damage and to examine the distribution of types of damage below the thermal level; and, (c) the influence of microwave frequency in the production of teratogenesis and thereby obtain data to help identify possible mechanisms for the non-thermal effects already observed.

PROGRESS/SIGNIFICANT RESULTS: 100% pupal mortality is observed for incident power levels of 320 mW at 9.0 GHz. This corresponds to a measured pupal temperature of 39.9°C. The 50% survival point lies between 160 mW (30.6°C) and 320 mW. This demonstrates that the previous results (1,2) were at power levels two to three orders of magnitude below the thermal kill range.

Two classes of pupa seem to exist: those more susceptible to microwave induced teratogenesis, and those that are less.

There is a close correlation between normal healthy pupae ("ideals") and slightly abnormal or damaged ("nonideal") pupa and the incidence of induced teratogenesis. Previously weakened insects are more susceptible to microwave damage.

There exists a "power window" where the microwave teratogenic effect is suppressed.

Measurements taken so far, indicate that microwave power absorption by a pupa is a strong, monotonically increasing function of frequency.

TITLE: Erythroid Effects of Radiation in the 1.0 R Range

GRANT NO: FD 00800-03

GRANTEE: SUNY at Buffalo
Albany, New York

PRINCIPAL INVESTIGATOR: Joseph K. Gong

ACTIVE DATE: 9/1/76 - 11/30/79

TOTAL SUPPORT: $88,023

FY 1978 SUPPORT: $41,722

OBJECTIVES: A recent study demonstrates that an acute x-ray dose of 1.0 R can induce erythroid changes in the bone marrow of the rats. The change observed between 10 days and 10 weeks following exposure, manifested as an increased level of normoblasts measured as a per cent of nucleated marrow cells in stained marrow smears, and as the number of normoblasts per mgm of isolated marrow, per whole femur and per total skeleton. When assayed at six or ten weeks post irradiation under induced anemic conditions (81 hours post phlebotomy) the fraction of increase in the number of normoblasts in the skeletons of the exposed subjects was only approximately one-half of that of the control animals. This indicates that 1.0 R irradiation had reduced the erythroid response capacity of the marrow of the exposed rats by one-half of its normal level. It was further observed that the reduced capacity of erythroid response was repaired at a rate of approximately 50% per 30 weeks. Because this is the dose level of radiation that urgently needs to be critically analyzed for health hazard evaluation and because this assay can be made in a very critical organ with relatively few animals, this in vitro marrow model would be ideal for the study of the effects of low dose radiation. The investigators propose to employ this model: (1) to determine the lowest dose of an acute and the lowest dose-rate of a continuous irradiation capable of inducing a biological effect; (2) to characterize the dose-response relationship in animals exposed to radiation dosages in the range of 1.0 R and lower; (3) to examine if a dose of radiation too low to elicit a detectable response can, when given repeatedly, ultimately induce a measurable change; and, (4) to determine the rate of recovery of the deficit erythroid response induced by acute irradiation. The results obtained will yield information that will be of direct use (without extrapolation) in the determination of the exposure limitations of low dose radiation.

PROGRESS/SIGNIFICANT RESULTS: Previously, single acute x-ray doses of 150, 550, 770 and 1500 mR given 6, 13 or 30 weeks earlier was shown to consistently induce changes in the marrow of the Sprague-

Dawley rats, while marrow of rats exposed to 50 mR invariable exhibited no detectable abnormalities. Currently, rats exposed repeatedly to 25 or 50 mR for total doses of 50, 100 or 150 mR during a period of 7 days were assayed one month following the last exposure. The purpose was to determine if there were latent hematopoietic effects too low for detection with our model associated with the individual "subthreshold" (25 and 50 mR) doses which can be summated to yield measurable changes.

In both experiments four erythropoietic parameters, the % of normoblasts (RBC$_p$ %), and the number of normoblasts per mgm marrow, per whole femur and per skeleton were examined one month post completion of the irradiation schedule. All four parameters showed similar responses; namely, all were above normal (t-test, $P<.05$) among subjects exposed to a total dose of 100 or 150 mR, given either as single or fractionated doses and with doses totaling 25 or 50 mR these measurements were similar to those of the sham-exposed animals. For example, the RBC$_p$ % of 50 mR received in two exposures, 50 mR rceived in one exposure and 25 mR received in one exposure with values ranging from 23.7 + .6 to 24.6 + .5 were similar to the 23.8 + .6 of the sham-irradiated rats. On the other hand, 100 mR received in four exposures, 100 mR in two exposures, 150 mR in three exposures, 100 mR received in one exposure and 150 mR in one exposure (total doses of 100 and 150 mR) with values ranging from 25.9 + .7 to 27.2 + .5 were all significantly higher than the sham-exposed values of 23.8 + .6.

It is concluded that doses such as 25 and 50 mR which by themselves are unable to elicit measurable marrow changes, when repeatedly given to yield a total dose of 100 mR or higher, can result in alternative changes similar to those detected in marrow exposed to an acute dose of at least 100 mR.

The finding that "subthreshold" doses are additive implies that the "threshold theory" or radiation effects may not be valid, and that the existence of the "linear hypothesis", at least within the limitations of the present model and dose range employed, is strongly suggested.

TITLE: Evaluation of PEID Systems for Radiology

GRANT NO: FD 00803-03

GRANTEE: University of Arizona
Tucson, Arizona

PRINCIPAL INVESTIGATOR: M. Paul Capp

ACTIVE DATE: 6/1/76 - 5/31/79

TOTAL SUPPORT: $191,369

FY 1978 SUPPORT: $101,945

OBJECTIVES: The objective of this project is the evaluation of photoelectronic imaging devices as used in radiology, which includes x-ray intensifiers, storage devices, video cameras and displays. Its purpose is to ensure that by proper evaluation (and the setting up of uniform procedures to make the evaluation) that minimal dose will be delivered to the human during exposure for x-ray radiographs.

PROGRESS/SIGNIFICANT RESULTS: To ensure continuity between methods of evaluation used for film and x-ray sensitive screens on the one hand and x-ray intensifiers on the other, considerable effort has been expended to measure precisely the quantum efficiency and gain of x-ray screens. The results were surprising and have important ramifications for efforts to use such screens as the sensor in x-ray cameras for diagnostic radiology.

These cameras are used in the emerging nations where their substantially lower cost makes them attractive compared to large x-ray intensifiers or large format film-screen systems. However, they generally require much higher dose levels than is acceptable in the United States. With significant improvement in components, they might well achieve an acceptable dose requirement even for the United States, and deliver satisfactory radiology at a substantially reduced cost.

The investigators have found for the best of the new rare earth screens that the gain in photons of light emitted per x-ray absorbed is in the range of 800 - 1000. When this gain is considered with the other factors that govern the operation of a conventional x-ray camera (namely the quantum efficiency of the optics and the photocathode used in a low light level image intensifier), it is clear that performance is improved over the past but remains marginal. The x-ray camera will still require more dose than the x-ray intensifier for the same quality radiograph. Either phosphor gain must be increased further, or the combined optics - low light level intensifier - must show better quantum efficiency.

TITLE: Biologic Responses to a Chronic Microwave Environment

GRANT NO: FD 00824-03

GRANTEE: University of Texas
Dallas, Texas

PRINCIPAL INVESTIGATOR: Robert M. Lebovitz

ACTIVE DATE: 5/1/76 - 4/30/79

TOTAL SUPPORT: $283,430

FY 1978 SUPPORT: $79,318

OBJECTIVES: The basic aim of this project will be to determine the effects of a long term (4 months) exposure to microwave radiation (MWR) at low incident power densities. The investigator's intent will be to examine behavioral, adrenocortical, and serotonin related effects of administratively safe MWR (i.e., less than 10 mW/cm^2 incident power density). Data will be obtained from several behavioral and biochemical 0-20 mW/cm^2. The chronic MWR environment will comprise a set of individual irradiation/test chambers into which control and experimental animals will be introduced for eight hours of whole body MWR exposure per day. Pulse modulated MWR at 1.2 GHz will be used. In the first part of this study, the effects of 0, 10, and 20 mW/cm^2 MRW on open field behavior and on instrumental behavior for food reward will be determined in rats. Besides the 0 mW/cm^2 group, an additional control group will be exposed to a mild thermal stress. In a later part of this study and to initiate the extrapolation of the results to human exposure, the instrumental behavior of monkeys for reward during chronic MWR will be determined. Again, dose-response curve will be defined via radiation at 5, 10, and 20 mW/cm^2 with dual control groups, as above. Coincident with these behavior studies, 24 hour urine samples of selected subgroups of rats and monkeys will be quantitatively analyzed for stress-related steroid fractions and/or for excreted 5-hydroxyindoleacetic acid. These studies will provide new and needed data regarding the extent to which low level MWR specific effects can be understood as secondary to mild thermal stress. A pattern of MWR specific responses that departs from that induced by ambient thermal stress, under identical conditions, would suggest that the results of chronic MWR encompass more than a hypothalamic reaction to hermogenesis. Null or negative results would enable us to more critically evaluate the extent of the risk derived from chronic whole body MWR exposure of the adult animal.

PROGRESS/SIGNIFICANT RESULTS: The first year of this study was spent in development of the exposure facility and the behaviorial apparatus and associated microprocessor based instrumentation to carry out this project. The complexity of the set-up required a year of development and testing. Data is now being collected, but the complexity and number of animals involved has not yet reached the point of reportable results. The data from these studies will provide data necessary for the reliable assessments of the behavorial consequences of chronic exposure to pulsed microwave radiation.

TITLE: Retinal Damage Caused by Chronic Exposure to Light

GRANT NO: FD 00874-03

GRANTEE: University of Louisville
Louisville, Kentucky

PRINCIPAL INVESTIGATOR: Theodore Lawwill

ACTIVE DATE: 9/1/76 - 8/31/78

TOTAL SUPPORT: $231,827

FY 1978 SUPPORT: $97,760*

OBJECTIVES: This research project is designed to determine thresholds for retinal damage from chronic exposure to light, in single exposures of four hours and in multiple exposures. The damage will be evaluated by functional testing with electroretinography and histological and pathological evaluation. The mechanisms of damage in this model will be studied by histological and biochemical techniques.

PROGRESS/SIGNIFICANT RESULTS: Damage is to be evaluated by functional testing with electroretingography and histological and pathological evaluation. Mechanisms of damage is being studied by histological and biochemical techniques.

Significant findings to date have been that light intensities which cause threshold damage in four-hour continuous exposures cause similar damage when applied for four one-hour periods at twenty-four hour intervals. It has also been shown that differences exist in the threshold values for retinal damage at 457.9, 514.5, and 590nm.

The findings of this study, particularly relating structural damage to functional damage could be very important information to BRH in assessing and setting of safety standards.

*Estimated Total Cost

TITLE: A Study of the Radiographic Aspects of Xeroradiography

GRANT NO: FD 00877-02

GRANTEE: Vanderbilt University
Nashville, Tennessee 1/

PRINCIPAL INVESTIGATOR: Gopala U. Rao

ACTIVE DATE: 9/1/76 - 8/31/79

TOTAL SUPPORT: $131,583*

FY 1978 SUPPORT: $45,298

OBJECTIVES: This is to study the physical aspects of xeroradiography and the correlation between dose, image quality and diagnostic accuracy.

PROGRESS/SIGNIFICANT RESULTS: Edge enhancement is the primary mechanism by which diagnostic information is conveyed in xeroradiography. Therefore, to analyze the influence of radiographic parameters on xeroradiographic images, it is first necessary to understand edge enhancement's interaction with factors such as contrast and radiation exposure.

They have demonstrated that there exists an optimal value for x-ray exposure transmitted through the patient for which the amount of edge enhancement is maximal. Based on this concept, a procedure for introducing automatic exposure termination in xeroradiography was developed.

In dosimetric studies using a phantom breast, the optimal skin exposures at 40 kVp were found to be 3.3, 15, and 43 Roentgens at magnification factors of 1x, 2x, and 3x respectively. These numbers decrease considerably with increase in kVp. From this it can be seen that at kilovoltages, magnification techniques are indeed possible without undue increases in radiation exposure.

*Estimated Total Cost

1/ Transferring to Medical College of Virginia, Richmond, Virginia; effective 9/1/78; the new number is 7 R01 FD 01004-01

TITLE: Ultrasonic Dosimetry

GRANT NO: FD 00927-01

GRANTEE: University of Illinois
Urbana, Illinois

PRINCIPAL INVESTIGATOR: William D. O'Brien, Jr.

ACTIVE DATE: 5/1/78 - 4/30/80

TOTAL SUPPORT: $57,722

FY 1978 SUPPORT: $57,722

OBJECTIVES: The principal objective of the research is to develop an ultrasonic dosimetric model or models from which the ultrasonic energy being absorbed by or interacting with tissue can be determined. The emphasis will be to define physical quantities which properly reflect an ultrasonic energy deposition in situ based upon knowledge of the free field distribution and ultrasonic propagation properties of the materials.

The second objective is to develop a dosimetric format by which patient exposure and particular organ and other body site exposure to ultrasonic energy is determinable. The anticipated format would be in terms of a quantitative parameter, or parameters, and would be useful in any subsequent retrospective or prospective epidemiology study.

The basic procedure will be to account for all of the ultrasonic energy when a specimen is irradiated. This will be accomplished by measuring the detailed ultrasonic field distribution patterns in the free field, in the field with the specimen in place and within the specimen. The measurement procedures include three absolute techniques and one relative technique. The specimens include phantoms of known acoustical properties and the biological tissues, testis, liver and kidney.

PROGRESS/SIGNIFICANT RESULTS: This study has not been in effect sufficient time to produce meaningful results.

TITLE: Electromagnetic Radiation and Biological Systems

GRANT NO: FD 00963-01

GRANTEE: Jerry L. Pettis Memorial VA Hospital
Loma Linda, California

PRINCIPAL INVESTIGATOR: W. Ross Adey - 1/

ACTIVE DATE: 3/1/78 - 2/28/81

TOTAL SUPPORT: $110,659

FY 1978 SUPPORT: $110,659

OBJECTIVES: Effects of weak environmental electric radiations (UHF and ELF) on biological systems are being investigated in a series of experiments ranging from neurochemical processes in isolated nervous tissues (chicks and cats), to EEG studies and concurrent development of implantable glass electrodes (chicks and cats), and to behavioral changes in laboratory animals (chicks, ducks and monkeys). Interaction of nervous tissue with extremely weak fields can not be adequately explained by classic models of neuronal excitability which involve far greater extracellular energies. Theoretical modeling of interaction, based on physical properties of the neuronal membrane (long range correlation and biological cooperativity) suggests new possibilities for brain information processes and detection of weak extracellular signals, not necessarily requiring synaptic activation. The role of intrinsic electric fields and associated electric noise in the CNS are being investigated. Implantable electric field probes (designed by the Research Group of the Division of Electronics Products, Bureau of Radiological Health (BRH) will be tested in anesthetized cats in order to establish preliminary, in vivo, measurements of field distributions within the head.

PROGRESS/SIGNIFICANT RESULTS: Neurochemistry - Major problems studied include:

1. Effects of changing incident energy of a 450 MHz field amplitude - modulated at 16 Hz on efflux of $^{45}Ca^{2+}$ from freshly isolated chick cerebral hemisphere. These studies have disclosed a power "window" in the sensitivity of cerebral tissue to these fields.

2. Effects of altered concentrations of hydrogen ions, bicarbonate ions and calcium ions in the cerebral extracellular fluid on tissue binding of $^{45}Ca^{2+}$ ions, with and without 450 MHz field exposure. Changing concentrations of calcium ions had little effect on efflux of $^{45}Ca^{2+}$ in the absence of the RF field, and did not interfere with the tissue responses to the imposed field. On the other hand, altered bicarbonate ion concentrations sharply altered $^{45}Ca^{2+}$ efflux

---

1/ This project was previously supported at UCLA with Suzanne M. Bawin as principal investigator - June 17, 1974 - November 1977. Total Support - $400,987.

and subsequent response to field exposure. Increased H^+ ion levels increased field sensitivity. These findings support models of transductive coupling based on competitive binding of calcium and hydrogen ions at membrane surface binding sites, as discussed below.

3. Evaluation of membrane surface sites in transductive coupling of weak modulated 450 MHz fields by the introduction of lanthanum ions, which block transmembrane movement of Ca^{2+} ions, and thus confine any observed field interactions to calcium bound at membrane surface sites. Our experiments have shown clear responses to the RF fields after tissue treatment with lanthanum. The findings suggest a class of electrosensitive membrane surface binding sites for calcium.

4. Sensitivity of calcium binding in awake cat cerebral cortex to weak modulated 450 MHz fields. Strong but not conclusive evidence has been found for increased $^{45}Ca^{2+}$ efflux from the surface of cerebral cortex in awake, immobilized cats. However, spontaneous shifts in states of arousal, with associated changes in metabolic CO_2 production, occur during efflux sampling, and must be excluded from these experiments to allow unequivocal evaluation of radiation effects.

Behavioral Studies - Influence of 450 MHz fields modulated at EEG frequencies on scheduled behavior of chicks:

Chicks were exposed to 450 MHz fields amplitude modulated at 3 or 6 Hz at low power (1 to 5 mW/cm^2) while performing on a Fixed Time (30 sec) Schedule for a 2.0 sec water reinforcement, which was in no way dependent upon the subject's behavior. Computer analyses of the recorded activity suggested differences in he temporal distribution of movements between field-on and field-off situations. These differences approached statistical significance.

Biophysical Models of Tissue Interactions with Weak High Frequency Electromagnetic Fields:

Research supported by this contract has disclosed for the first time a series of non-equilibrium interactions between 147 and 450 MHz fields and brain tissue. Indications that these interactions are, indeed, resonant atomic or molecular reactons were found in their restriction to narrow frequency and amplitude "windows". Our detection of these restricted interactions has been confirmed in independent studies by Blackman, et al, in the Environmental Protection Agency. They are amongst the first clear instances of biological cooperative processes. Their biophysical substrates are not known. Models so far proposed have considered the polyanionic character of membrane surface glyco-proteins and glycolipids. These models have proposed an ordering of long-range fixed charge interactions. We are currently developing such a model in which mobility of hydrogen ions would provide a basis for proton "tunneling" along membrane surfaces.

TITLE: Health Consequences of Nasopharyngeal Radium Exposure

GRANT NO: FD 00977-01

GRANTEE: Johns Hopkins University
Baltimore, Maryland

PRINCIPAL INVESTIGATOR: Genevieve M. Matanoski

ACTIVE DATE: 5/1/78 - 4/30/79

TOTAL SUPPORT: $27,579

FY 1978 SUPPORT: $27,579

OBJECTIVES: This is a new project for the follow-up of persons exposed to radium irradiation for treatment of enlarged adenoids to determine the existence of any disease risks due to low-dose radium exposure.

PROGRESS/SIGNIFICANT RESULTS: This study has not been in effect long enough to have produced any results at this time.

This grant application describes a well designed community based study of possible delayed effects of radium treatments for enlarged adenoids and tonsils of children and adolescents. Results of this study would be important to BRH as regards the following:

The procedure was very common and a decision needs to be made as to whether to advise follow-up of all persons who as children were treated with radium. The study will provide an estimate of possible effects of relatively low levels of exposure to radium which emitted primarily gamma and beta rays. Estimated exposures of radiosensitive tissues include up to 48R to the thyroid and 6 to 120R to the pituitary and parotid glands. The study may throw light on the important question of possible indirect effects of irradiation of the pituitary gland. There has been only one study which was about half the size of the present study and it did not show an increased risk of cancer from a similar radium exposure (Hazen et al. 1966). Thus this well conceived study with good dosimetry is needed.

A special feature of the proposed study is the ability to compare the level of reporting thyroid tumors and surgery on a mail questionnaire with actual hospital reports for residents of an entire county. The results of this evaluation will be useful to the Bureau study of subjects who as children received I-131 for diagnosis of thyroid disease.

Mr. ROGERS. What about your intramural program?

Mr. VILLFORTH. The intramural program is primarily nonionizing radiation in terms of bioeffects and in terms of dosimetry; that is, the science of measurement. In the Bureau, mostly nonionizing radiation. The reason being, as we look around the Federal Establishment, there are not that many agencies doing work in light radiation, lasers, ultrasound, microwave, and RF.

Mr. ROGERS. Are we doing a sufficient amount?

Mr. VILLFORTH. In terms of the total Government doing sufficient amount, I guess the standard answer has to be there is always a need for additional resources in the total government to move faster in the bioeffects area and do more in the way of measurements.

Mr. ROGERS. Are we doing sufficient in food and drug?

Mr. VILLFORTH. In terms of the balance of efforts, I will let the Commissioner answer it.

Mr. ROGERS. In other words, do we need to beef up this budget, is what I am saying.

Dr. KENNEDY. I would say, in looking at that bureau in comparison with other FDA bureaus, I would say it is more research-intensive than most. However, compared with national research efforts and national needs in the areas of ionizing radiation research and biological effects of nonionizing radiation, I would say it is a bureau that could definitely use additional resources.

Despite the fact that it is already fairly research-intensive, I have given it some attention in the way of allocating discretionary funds because I think it has significant absorptive capacities. It is one of the best scientific organizations in our agency. I think it can do good work and make good use of research resources.

Mr. ROGERS. Would you let us have for the record what you think the budget should be in view of the overall problem.

[The following information was received for the record:]

IONIZING RESEARCH - 1980

Methods to quantify and evaluate the system performance of computed tomography (CT) and image intensified fluoroscopy will be developed. Dosimetry systems and methods to determine patient dose will be developed for CT. Fluoroscopy field test methods will be developed. Safety and efficacy studies of nuclear medicine procedures and devices will also be conducted.

System designs using x-ray spectra optimization and scatter reduction techniques will be evaluated. An analysis of imaging process, factors affecting process, and studies of special technological developments will be conducted to determine potentials and limitations. An epidemiological study will be developed to determine effects of long-term radiation therapy.

Risk/benefit cost analyses and prioritization of x-ray examinations will be performed. Research protocol and high yield patient selection criteria will be established for selected diagnostic exams.

ACTIVITY	POSITIONS	$1,000
Instrumentation & Product Evaluation Research	46	3,730
Bioeffects Research	3	240
Patient Selection Criteria Research	20	750
TOTAL	69	$4,720

NONIONIZING RESEARCH - 1980

Field measurement instrumentation and methods for evaluating light, sonic, and radiofrequency and microwave products will be developed. The physical parameters of emissions from these nonionizing electronic products will be assessed to determine the mechanisms of interaction with humans. Laboratory methods and measurement instrumentation, including necessary dosimetry, will be developed. Laboratory studies of the mechanisms of bioeffects from exposures to nonionizing products will be conducted. Various biological endpoint studies will be conducted to determine the hazards from these products. Populations at risk will be identified and appropriate epidemiological studies will be conducted of those exposed to nonionizing electronic products. Existing laboratories will be consolidated into a centralized facility.

ACTIVITY	POSITIONS	$1,000
Instrumentation and Product Evaluation Research	25	1,650
Bioeffects Research	13	1,200
Laboratory Facilities	--	340
TOTAL	38	$3,190

Mr. Rogers. What about intramural research, $1.6 million?

Dr. Kennedy. By intramural, outside grants and contracts?

Mr. Rogers. Yes. He said had a grants program and then a contract program of 1.6.

Dr. Kennedy. Yes.

Mr. Rogers. We have covered the grants of $312,000. What I am covering now is your intramural research not covered by your grant program; your contract program, in other words. Has that gone down or gone up?

Mr. Villforth. I think that has gone up. One must recognize that a significant portion of that $2.9 million is the beagle colony, almost 2,000 beagles out at Fort Collins; Colorada, on which we are doing a lifetime study. When you are halfway through a project that has a 20-year life and you have a commitment of several millions of dollars, we must run that out to the end.

Now that is increasing.

Mr. Rogers. How much?

Mr. Villforth. It is running about $1 million per year.

Mr. Rogers. So most of your contract work sustains the beagle project?

Mr. Villforth. Yes, sir. The single major portion of our contract work in ionizing radiation is to sustain the beagle colony.

Mr. Rogers. What other work is being done?

Mr. Villforth. The contract review and ionizing radiation is covered in more detail in what were submitted for the record.

Mr. Rogers. How many other contracts exist; intramural contracts other than the beagle?

Mr. Villforth. Approximately 30, without counting them.

Mr. Rogers. If you will specify those; principal investigator, how much, how long, how long it should extend, the subject matter and possible results.

Mr. Villforth. That is in here.

Yes, sir, that is for the record.

[Testimony resumes on p. 477.]

[The following information was received for the record:]

SUMMARY OF FDA/BRH ACTIVE RESEARCH CONTRACTS AND INTERAGENCY AGREEMENTS

The attached descriptions have been prepared for only those BRH contracts which have been classified as "research" as differentiated from "development" or "scientific support" types.

The selection does not include detailed descriptions of the following contracts which are listed by radiation source in order to more completely show the range of BRH contracting.

IONIZING

1. International Symposium on the Biological Effects of 224 Ra.
2. Simulation and Evaluation of Dose-Image Parameter Relationship for Computed Tomography Systems.
3. Design, Evaluation and Calibration of Mailable Dosimetric System for Measurement of Absorbed Dose in Phantom Material.
4. Evaluation Program for Imaging Collimators.
5. Nuclear Medicine Research Support Services.
6. Development of Quality Control Workshops for In-Vitro Nuclear Medicine.
7. National Conference on Educational Programs in Nuclear Medicine Technology.
8. Radiological Health Sciences Education Project.
9. Radiological Health Sciences Learning Laboratory Accession System.

NONIONIZING

1. Development of Laser Calorimeter.
2. Testing of Non-Coherent Light Sources.
3. Develop Standards and Methodology for Measuring Incoherent Light Sources.
4. Development, Testing, and Calibration of Three Prototype Field Portable Ultraviolet Radiation Hazard Monitors.
5. Development of Specifications for Computer Programs to Obtain Electromagnetic Fields in Dielectric Media of General Geometry.
6. Computer Studies of Dose Distribution in Biological Models Exposed to Electromagnetic Radiation.

MULTIPLE RADIATION SOURCES AND MISCELLANEOUS

1. Coordinate Federal/State Radiation Control Activities and Assist in Solving Radiation Control Problems.
2. Support of Training for Radiological Emergency Response Planning.
3. Research Animal Housing and Service.

TITLE: Determination of the RF Parameters that Affect the Brain and Behavior at Low Power Density

CONTRACT NO: 223-74-6040

CONTRACTOR: Randomline, Inc.
Huntington Valley, Pennsylvania

PRINCIPAL INVESTIGATOR: Allan H. Frey

ACTIVE DATE: 2/15/74 - 4/14/78

TOTAL SUPPORT: $185,146

FY 1978 SUPPORT: -0-

OBJECTIVES: To develop behavioral and brain assay techniques and explore with them the effects of electromagnetic radiation, particularly UHF and to some degree higher frequency radiation. To establish thresholds, determine effects of modulation, generalize the findings to species of various size, and determine chronic and long-term effects at low power densities.

PROGRESS/SIGNIFICANT RESULTS: Experiments showed a clean cut "docility" effect of exposure to EM energy in rats undergoing the stress of pain induced aggression procedure.

The exact nature of the effect and the appropriate level for the effect remains to be defined. The effect occurs at rather low power levels as such are defined in biological investigations of EM energy effects. The power levels used, however, are above what is generally found in the environment. The threshold for the EM energy parameters used is a peak power between 0.05 mW/cm^2 and 0.1 mW/cm^2. The measurements given, although exact, are considered to be correct within an order of magnitude because of the perturbing effect of the animal and any apparatus in the EM field.

Other experiments showed that pulsed modulated EM energy had an adverse effect on motor coordination or balance as defined by use of the rotating rod test.

The effect occurs at rather low power densities as this is usually defined in biological experiments. The threshold for the effect with the energy parameters used is a peak power between 0.4 mW/cm^2 and 2.8 mW/cm^2. The measurements given, although exact, are considered to be correct within an order of magnitude because of the perturbing effect of the animal and any apparatus in the EM field.

TITLE: Wavelength Dependence of Latent Tumor Virus Activation by Light

CONTRACT NO: 223-74-6067

CONTRACTOR: Western Kentucky University
Bowling Green, Kentucky

PRINCIPAL INVESTIGATOR: Thomas Coohill, Ph.D.

ACTIVE DATE: 6/1/74 - 9/29/78

TOTAL SUPPORT: $239,031

FY 1978 SUPPORT: -0-

OBJECTIVES: To determine the relative sensitivity of latent tumor virus to activation at different light wavelengths, with emphasis on near ultraviolet and visible light.

PROGRESS/SIGNIFICANT RESULTS: The contractor has investigated the wavelength dependence of tumor virus induction by light, especially in the near and far ultraviolet (UV) regions of the spectrum. Data collected shows that the most effective wavelength is 265 nm. Virus induction was observed at wavelengths up to 300 nm. The contractor has also shown that the ability of mammalian cells to replicate a suspected human tumor virus, herpes simplex, was decreased following treatment of cells with germicidal UV light or with near-UV light plus the photosensitizing drug psoralen. The wavelength dependence of UV light enhanced reactivation of herpes virus was examined and action spectra obtained. A detailed report of this research is available as a FDA technical report.

TITLE: Effects on Offspring of High Level Exposure to Microwave Radiation

CONTRACT NO: 223-75-6017

CONTRACTOR: American Health Foundation
New York, New York

PRINCIPAL INVESTIGATOR: Jeanne M. Stellman, Ph.D.

ACTIVE DATE: 6/30/75 - 9/30/78

TOTAL SUPPORT: $81,440

FY 1978 SUPPORT: -0-

OBJECTIVES: Assess the effects of microwave radiation exposure of individuals on the incidence of selected congenital malformations in their offspring.

PROGRESS/SIGNIFICANT RESULTS: A suitable study population has been identified. All clearances for this study have been obtained. OMB approval of the survey questionnaire has been obtained and questionnaire has been mailed. Approximately 20 percent return resulted from the first mailing and followup has been started. No results are available at this point.

TITLE: Program to Provide Current Internal Radiation Absorbed Dose Estimate Based on Human Data for Radioactive Pharmaceuticals Used in the Practice of Nuclear Medicine

CONTRACT NO: 223-75-6067

CONTRACTOR: Society of Nuclear Medicine
New York, New York

PRINCIPAL INVESTIGATOR: Edward M. Smith

ACTIVE DATE: 2/1/74 - 5/31/78

TOTAL SUPPORT: $46,100

FY 1978 SUPPORT: -0-

OBJECTIVES: Perform dose model calculations on biological dose data to provide Dose Estimate Reports for certain radionuclide compounds for dissemination to nuclear medicine practitioners.

PROGRESS/SIGNIFICANT RESULTS: Dose estimate reports have been prepared for ^{75}Se-L-Selenomethionine; ^{66}Ga-, ^{67}Ga-, ^{68}Ga-, and ^{72}Ga-Citrate; ^{99m}Tc-Sulfur Colloid and ^{198}Au-Colloidal to humans with various liver conditions; ^{123}I, ^{124}I, ^{125}I, ^{126}I, ^{130}I, ^{131}I, and ^{132}I as sodium iodide; ^{197}Hg and ^{203}Hg labeled Chlormerodin; ^{123}I, ^{124}I, ^{126}I, ^{130}I, and ^{131}I labeled Rose Bengal; ^{99m}Tc as sodium pertechnetate; specific absorbed fractions for photon sources uniformly distributed in various organs of a heterogeneous phantom; and kinetic models for absorbed dose calculations. These dose estimates are used as supporting data in the regulatory and advisory programs of the Bureau of Drugs, Bureau of Biologics, and Bureau of Radiological Health.

TITLE: Advisory Committee to the Radiation Registry of Physicians

CONTRACT NO: 223-75-6055

CONTRACTOR: National Academy of Sciences

PRINCIPAL INVESTIGATOR: Gordon Jessup, Ph.D.

ACTIVE DATE: 6/30/75 - 12/29/78

TOTAL SUPPORT: $10,000

FY 1978 SUPPORT: -0-

OBJECTIVES: To convene two meetings of the Advisory Committee which will critically review the current progress of the Radiation Registry of Physicians project to ensure conformance with project objectives and to evaluate the continuity and adequacy of data collection and analysis procedures. To provide guidance and recommendations for work in progress and/or work to be performed in the immediate future. To publish any required materials dealing specifically with the Radiation Registry of Physicians as needed and requested by the Government in order to ensure the completeness of data collection.

PROGRESS/SIGNIFICANT RESULTS: One meeting of the Advisory Committee was held on October 12, 1976, at which time some preliminary analyses of data was presented. The Committee raised a number of questions with respect to the deviation of the data and the questionnaires used to obtain the raw data. There was discussion of the interpretation of the analyses. In as much as analysis was incomplete at that time, no conclusions were reached. A number of recommendations were made by the Committee for future analysis. A publication manuscript has been prepared on "Personal Usage of Medical Radiological Procedures by Radiologists, Pathologists, and Their Families". Revisions to this manuscript following review are underway. A joint meeting of the BEIR Committee and the Advisory Committee is tentatively scheduled for the fall of 1978.

TITLE: A Followup Study of Persons Who Had ^{131}I and Other Diagnostic Procedures During Childhood

CONTRACT NO: 223-76-6053

CONTRACTOR: Research Triangle Institute
Research Triangle Park, North Carolina

PRINCIPAL INVESTIGATOR: Benjamin S. H. Harris, III

ACTIVE DATE: 9/15/76 - 9/14/79

TOTAL SUPPORT: $549,241

FY 1978 SUPPORT: -0-

OBJECTIVES: Identify, locate, followup, and ascertain general health status in persons exposed to diagnostic ^{131}I during childhood, along with two control groups.

PROGRESS/SIGNIFICANT RESULTS: This multi-institutional study is in the early stages of data collection. The results should provide a basis for evaluation established medical practice and national environmental emission standards. There are presently 15 hospitals actively participating in this survey with a number of other potentials. Abstracting of hospital records is underway at all 15 active participants. No results are available at this time.

TITLE: Controlled Followup Study of Persons Treated for Thyrotoxicosis with Therapeutic Iodine-131 or Surgery

CONTRACT NO: 223-77-6004

CONTRACTOR: Mayo Foundation
Rochester, Minnesota

PRINCIPAL INVESTIGATOR: Leonard T. Kurland, M.D.

ACTIVE DATE: 7/11/77 - 7/10/78

TOTAL SUPPORT: $24,550

FY 1978 SUPPORT: -0-

OBJECTIVES: The study will follow up patients treated with Iodine-131 and treated surgically for hyperthyroidism to determine whether exposure is related to an increased risk of mortality and morbidity, particularly that due to cancer.

PROGRESS/SIGNIFICANT RESULTS: This controlled followup will add 10 years of observation to the cooperative thyrotoxicosis therapy followup study which was completed in 1968. It may permit an evaluation of the cost-effect characteristics of I-131. All abstracting of patients's records is complete. Survey questionnaire has been mailed with approximately 60 percent response thus far. Followups are about 50 percent complete. Validation studies will begin following completion of all questionnaire followups. No results can be reported at this time.

TITLE: Comparison of Iodine and Technetium-99m as Imaging Agents for Thyroid Studies

CONTRACT NO: 223-77-6012

CONTRACTOR: Michael Reese Medical Center
Chicago, Illinois

PRINCIPAL INVESTIGATOR: Steven M. Pinsky, M.D.

ACTIVE DATE: 10/1/77 - 9/30/78

TOTAL SUPPORT: $12,500

FY 1978 SUPPORT: -0-

OBJECTIVES: Conduct comparative studies of the efficacy of 1-123 as sodium iodide and technetium as sodium pertechnetate for thyroid imaging in patients with known abnormalities of the thyroid gland.

PROGRESS/SIGNIFICANT RESULTS: All clearances and approvals required for human subject studies have been obtained. Of a total expected examination on 100 patients, there have been 79 patient studies. All patients studied have had palpable nodules or other obvious abnormalities of the thyroid. Each patient has been studied using Technetium-99m and Iodine 123. Medical histories have been supplied for each patient. Because this study is incomplete, no analysis of the findings to date has been made and therefore no significant trends or results can be reported at this time.

TITLE: Self-Assessment and Competency Assurance Education in Diagnostic Radiologic Technology

CONTRACT NO: 223-77-6013

CONTRACTOR: American Society of Radiologic Technologists
Chicago, Illinois

PRINCIPAL INVESTIGATOR: Ward M. Keller

ACTIVE DATE: 9/30/77 - 9/29/79

TOTAL SUPPORT: $223,170

FY 1978 SUPPORT: -0-

OBJECTIVES: Provide a system to assess competency of individuals and develop profiles of deficiencies in order to better plan and implement continuing education and training of both noncredentialed and credentialed radiographers.

PROGRESS/SIGNIFICANT RESULTS: Identification of volunteer radiographers to participate in the educational program is in progress. The self-assessment test is scheduled for review and administration.

TITLE: Assessment of Repeat Examinations in Nuclear Medicine

CONTRACT NO: 223-77-6014

CONTRACTOR: Small Business Administration
(J. Robb Assoc. - Subcontractor)
Dallas, Texas

PRINCIPAL INVESTIGATOR: Cornelius Askew, Jr., Dr.PH

ACTIVE DATE: 9/30/77 - 9/29/78

TOTAL SUPPORT: $15,395

FY 1978 SUPPORT: -0-

OBJECTIVES: Determine the frequency of repeat examinations in nuclear medicine, the factors contributing to these repeats, and the relationship between repeats and type of examination.

PROGRESS/SIGNIFICANT RESULTS: A survey form has been designed to record the necessary information, and data is being collected which will serve as a basis for the repeat examination survey.

TITLE: Design and Develop a Portable Ultrasonic Therapy Wattmeter

CONTRACT NO: 223-77-6015

CONTRACTOR: Anatole J. Sipin Co.
New York, New York

PRINCIPAL INVESTIGATOR: Anatole J. Sipin

ACTIVE DATE: 9/30/77 - 10/31/78

TOTAL SUPPORT: $24,374

FY 1978 SUPPORT: -0-

OBJECTIVES: Design and develop a portable ultrasonic wattmeter to provide accurate calibration of ultrasonic therapy equipment and to provide for the commercial availability of such instrument.

PROGRESS/SIGNIFICANT RESULTS: An instrument which can measure the total temporal average ultrasonic power from ultrasonic therapy equipment is near completion.

TITLE: Development of a Diagnostic Ultrasound Training Phantom

CONTRACT NO: 223-77-6017

CONTRACTOR: University of Colorado Medical Center
Denver, Colorado

PRINCIPAL INVESTIGATOR: Paul L. Carson, Ph.D.

ACTIVE DATE: 9/26/77 - 9/25/78

TOTAL SUPPORT: $46,473

FY 1978 SUPPORT: -0-

OBJECTIVES: Design and construct a model of the human torso which, when scanned by a diagnostic ultrasound scanner, would yield an ultrasonic image equivalent to a typical scan of normal human anatomy in the abdomen.

PROGRESS/SIGNIFICANT RESULTS: Materials have been tested and selected for construction of various organs of the phantom. Experiments have begun to determine appropriate molding techniques.

TITLE: Analysis of Factors Which Affect the Performance of Medical X-Ray Equipment Operators

CONTRACT NO: 223-77-6018

CONTRACTOR: Small Business Administration
(Uniworld Group - Subcontractor)
New York, New York

PRINCIPAL INVESTIGATOR: Jacques P. Guerin and Susan W. Morris

ACTIVE DATE: 9/30/77 - 12/29/78

TOTAL SUPPORT: $122,099

FY 1978 SUPPORT: -0-

OBJECTIVES: Provide current national indices of the relationships between certain background characteristics such as work environment, attitudes, and practices of medical x-ray equipment operators to constitute a data base for informed planning of radiological health programs by Federal, State, local and professional organizations.

PROGRESS/SIGNIFICANT RESULTS: The design of the study was based on information from the results of a pilot study conducted in 1976. The plan for validation of the performance measures has been completed and the analysis plan is being refined. The respondent questionnaire has been revised and submitted for OMB clearance.

TITLE: Evaluation of Somatic Doses from Diagnostic Radiology

CONTRACT NO: 223-77-6023

CONTRACTOR: Dickinson College
Carlisle, Pennsylvania

PRINCIPAL INVESTIGATOR: Priscilla Laws, Ph.D.

ACTIVE DATE: 9/30/77 - 9/29/78

TOTAL SUPPORT: $15,053

FY 1978 SUPPORT: -0-

OBJECTIVES: Determine somatic doses to internal organs from diagnostic radiology procedures, evaluate the feasibility of adopting exposure limits for such procedures, and determine the variation in somatic doses as a function of competing techniques or practices.

PROGRESS/SIGNIFICANT RESULTS: The progress thus far has consisted of: (1) collecting data on a variety of radiation exposure limits and beginning to study the relationships between medical practice and these parameters; (2) specific x-ray projections have been selected and the variation of somatic doses as a function of these techniques has been studied; (3) expected dose reductions as a function of kVp for the PA chest, AP lumbosacral spine and AP abdomen are being calculated; and, (4) dose reductions as a function of the facility type for these three exams are being calculated. The detailed development of the radiation detriment concept is progressing with current effort devoted to formulation of the genetic component of total detriment.

TITLE: Statistical Analysis of Data Collected in the Oxford Survey of Childhood Cancers

CONTRACT NO: 223-77-6026

CONTRACTOR: University of Birmingham
Birmingham, England

PRINCIPAL INVESTIGATOR: Dr. Alice Stewart, M.D.

ACTIVE DATE: 6/30/72 - 9/28/78

TOTAL SUPPORT: $278,339

FY 1978 SUPPORT: -0-

OBJECTIVES: Use the collected Oxford Survey data to study human radiosensitivity, the process which enables radiation to cause cancers.

PROGRESS/SIGNIFICANT RESULTS: Prenatal exposure to low radiation doses (0.5 to 2 rads) is associated with a 40-50 percent increase in risk of childhood leukemia and possibly the same level of increased risk for all childhood cancers. Findings from this study are a basis for present recommendations for the use of radiation in pregnancy. Extensive data analysis has been made to rule out extraneous factors such as social class, birth weight, reasons for maternal x-rays, etc. Better estimates of the true risk of exposure will result from analyses now underway. Children who died of leukemia were found to have had, on the average, more episodes of infective diseases than children who died of solid tumors or the surviving controls.

TITLE: Calculation of Internal Organ Doses From External X-Ray Exams

CONTRACT NO: 224-72-6024

CONTRACTOR: Department of Energy
Oak Ridge National Laboratory
Oak Ridge, Tennessee

PRINCIPAL INVESTIGATOR: Gordon Warner

ACTIVE DATE: 3/1/72 - 9/30/78

TOTAL SUPPORT: $266,000

FY 1978 SUPPORT: $25,000

OBJECTIVES: To develop a technically sound calculational procedure for determining the average absorbed dose in several critical organs (gonads, bone marrow, thyroid, lens of eye) per unit of incident radiation exposure for normally and obliquely incident external x-ray beams in the average range 20-150 KeV to develop a complete basic data file for routine calculation of internal organ doses from external x-ray beams in the medical diagnostic range; and to develop a flexible and independent general BRH capability to calculate internal organ doses for non-routine dose estimation.

PROGRESS/SIGNIFICANT RESULTS: A calculational technique for computer use in obtaining absorbed doses to internal organs was developed and put into use. A large number of organ dose computations at various energy levels have been done resulting in the publication of a handbook of organ doses and a users handbook for adult patients. A pediatric phantom was developed and organ dose calculations based on it have been completed.

A pediatric organ dose handbook is in the process of publication. Future plans include the preparation of a mammography handbook.

TITLE: Applying Microcalorimetric Techniques to Monitor Changes in Physiological Status in Biological Systems Resulting From Ionizing Irradiation and Other Physical Stresses

CONTRACT NO: 224-77-6015

CONTRACTOR: National Bureau of Standards
Washington, D.C.

PRINCIPAL INVESTIGATOR: Edward Prosen

ACTIVE DATE: 9/1/77 - 9/30/78

TOTAL SUPPORT: $15,000

FY 1978 SUPPORT: $7,500

OBJECTIVES: To design and construct a microcalorimeter to be used specifically for measuring metabolic heat and oxygen uptake patterns in alpha-irradiated and control fertilized arbacia ova. Changes in normal cleavage time or the arrest in any stage of development will be observed.

PROGRESS/SIGNIFICANT RESULTS: The cell research calorimeter has been designed. Special quartz reaction vessels have been fabricated and are being tested. A sensitive quartz pressure gauge has been modified and is being tested for Warburg-type cell respiration studies. The observation of anomalous cleavage patterns in the fertilized arbacia ova is being investigated.

Mr. ROGERS. What do you intend to show from the beagle project?

Mr. VILLFORTH. I think the beagle project is an extremely exciting project because it relates very much to the subject we talked about earlier; that is, the question of pelvimetry or the question of radiation during pregnancy, because the purpose of the project is to examine if there are different effects from a comparable amount of radiation received at different times after conception of the beagle. This should get some hint as to some——

Mr. ROGERS. Have you had any results yet?

Mr. VILLFORTH. We have had some preliminary results.

Mr. ROGERS. But you are showing basically what?

Mr. VILLFORTH. We are showing an increased number of certain types of cancers.

Mr. ROGERS. Will you let us have whatever is shown to date?

Mr. VILLFORTH. Yes, sir, keeping in mind it is too soon to have statistical correlation of that.[1]

Mr. ROGERS. How many people actually go out and inspect devices, X-rays or microwave? Do you do much of that, or is your manpower too short?

Mr. VILLFORTH. It depends on the nature of the manufacture from one to two, and I guess I would be facetious, partially facetious, and say when the manufacturer of the laser group at Wolf Trap on Saturday presented the laser show, there were at least 12 of us out there.

Mr. ROGERS. In the audience or inspecting?

Mr. VILLFORTH. Four of us in the audience.

Mr. ROGERS. I hope you didn't get zapped.

Mr. VILLFORTH. The number depends on the complexity of the manufacture, the number of products.

Mr. ROGERS. Suppose you inspect a machine in the field and find it out of compliance; how do you assure it is brought into compliance?

Mr. VILLFORTH. If we are talking about an X-ray machine in which the non-compliance is a result of the assembler as opposed to a problem identified by the primary manufacture, that is a problem that would appear to be inherent in all of those machines. But if it is one with the assembler, then the assembler is notified, the user is aware of the situation and, depending on the nature of the situation, one could shut the machine down or one could get the assembler in to correct the problem.

Mr. ROGERS. Do you have the authority to shut the machine down?

Mr. VILLFORTH. We don't have the authority to shut the machine down—in a situation like that, working with the State health department, if there was a question of public health——

Mr. ROGERS. Your have to depend on a State authority?

Mr. VILLFORTH. Yes.

Mr. ROGERS. Should you have that authority?

---

[1] The beagle project referred to is contained in a report entitled CSU-FDA Collaborative Radiological Health Laboratory annual report 1977, and may be reviewed in the subcommittee files.

Mr. VILLFORTH. I won't pursue that. We will let the Commissioner answer that.

Mr. ROGERS. Should you have such authority?

Dr. KENNEDY. I am not aware that there is a significant number of cases, indeed any cases, in which we have needed to shut down a machine and not been able to obtain cooperation or obtain an appropriate response to our request from the State health authorities.

Mr. ROGERS. How do you now, Commissioner? Because you are not even inspecting the machines, sir.

Mr. VILLFORTH. We are inspecting the machines.

Mr. ROGERS. How many?

Mr. VILLFORTH. It is just we are not inspecting all of them.

Mr. ROGERS. How many? You inspect 15 percent; isn't that what you told me? I am not sure that is a very good judgment to make on the basis of a 15 percent inspection.

Dr. KENNEDY. But that problem couldn't be changed by the additional authority to shut down, Mr. Chairman. It may very well be we are missing cases in which we would find recalcitrant machine operators or manufacturers.

Mr. ROGERS. It may mean you don't need inspections if you don't have the authority to do anything, so maybe the manpower is not needed for you, but simply for the State. That's the difference.

Dr. KENNEDY. That is correct.

Mr. ROGERS. So it does have something to do with it.

Dr. KENNEDY. We are increasing our State contract activity. I thought the purpose of your question, Mr. Chairman, was to ask if we needed authority to get the shutdowns accomplished. There we are not aware at this point that the lack of that authority has created a problem.

Mr. ROGERS. You have no problem closing down a machine?

Dr. KENNEDY. By and large, the people have been responsive to our requests.

Mr. ROGERS. Have there ever been any problems?

Mr. VILLFORTH. I am not aware of a situation that you describe.

Mr. ROGERS. None at all.

Mr. VILLFORTH. That's right.

Mr. ROGERS. If you find something wrong, you simply advise the state authorities and that problem is taken care of.

Mr. VILLFORTH. Yes. If there is a need for the machine to be shut down, yes, sir.

Mr. ROGERS. How do you tell what type of error it is when you have, and as the Commissioner earlier described, parts from maybe 10 manufacturers coming in? How do you identify who is responsible?

Mr. VILLFORTH. The person who assembles it or the assembler, in the case of multiple components from multiple manufacturers coming together, the person who is held responsible and, under our definition, is charged as a manufacturer.

Mr. ROGERS. Is this easily discernible?

Mr. VILLFORTH. He has to fill out assembler forms.

Mr. ROGERS. He sits on the machine. Is there any indication, when you go to check a machine, that that is put together or assembled? Is there any identifying code?

Mr. VILLFORTH. Each component has to be certified, so each component will have a certification label on it.

Mr. ROGERS. And that is easily discernible so you can tell if it has been assembled by different manufacturers or whether it is made by one manufacturer?

Mr. VILLFORTH. That's correct. Yes, that is correct.

The question you asked, though, about the assembly and whether or not the assembler might still misassemble it, one could still have certified components, so labeled, properly labeled and misassembled. The assembler must fill out an assembler form, which we then inspect the assembler against that from so we have a way of identifying here is a new machine or collection of components, you can go out and inspect.

You are right, this is a 15 percent inspection level; this gives us a pretty good cross-section. If one is a problem assembler, he doesn't assemble just one machine; he assembles many machines.

Mr. ROGERS. What about old machines brought back in, fixed up and resold; is that a problem?

Mr. VILLFORTH. If the X-ray machine is refurbished, it is treated as if it were newly manufactured and would require the same kind of inspection.

Mr. ROGERS. In other words, you have that fall under the requirements of the law; that is treated as a new machine?

Mr. VILLFORTH. Yes, we have some problems, of course, and that is the identification of what is the word "refurbish." You bring back an old machine and paint it and don't do anything to the electronics; is that refurbissing or not?

Mr. ROGERS. Do you have guidelines for that?

Mr. VILLFORTH. We have guidelines to the assemblers in a situation like that.

Mr. ROGERS. And manufacturers?

Mr. VILLFORTH. Not the manufacturers. The assemblers, not the primary manufacturers.

Mr. ROGERS. The primary manufacturers never bring back in those machines to be fixed?

Mr. VILLFORTH. We had a situation in the microwave oven area where that occurred. I am not aware of the X-ray manufacturers.

Mr. ROGERS. But you would consider them new machines and they would fall under the law?

Mr. VILLFORTH. Yes.

Mr. ROGERS. What happens when old or used equipment is sold from one practitioner to another?

Mr. VILLFORTH. In terms of the radiation control——

Mr. ROGERS. Who controls them?

Mr. VILLFORTH. We have no authority to check them. When a practitioner buys someone else's practice or buys an old machine or the widow sells a machine to a new physician, in general the States have a registration program. That information, the new recipient is required to register that with the State. It would come under the State inspection program.

I was going to say that the State, of course, is concerned beyond just the machine, per se. Even if it is a superb machine, all certified and put into a facility that is inadequately shielded, the walls of the facility are inadequately shielded, the State has a concern there. That is something that goes beyond our law.

Mr. **Rogers**. Would you let us have for the record, Mr. Commissioner, recommendations as to changes in the law which you think are necessary for the protection of the public on radiation?

Dr. **Kennedy**. We will be glad to do that, Mr. Chairman.

[Testimony resumes on p. 486.]

[The following information was received for the record:]

PROPOSED NEW AND EXPANDED LEGISLATIVE AUTHORITIES UNDER P.L. 90-602

A. Use Control Authority

1. Legislative Proposal: The Secretary shall be authorized to promulgate use and/or user controls to expand capacity for efficient enforcement of the Act. Specifically, the Secretary is directed to:

   (a) Establish minimum standards for facility quality assurance programs to be implemented by States;
   (b) Develop and conduct programs to inform medical and dental practitioners, as well as students, about the risks and benefits of medical radiation;
   (c) Develop minimum standards for adoption by State licensing and accreditation agencies for the certification of persons who conduct, prepare, or refer patients for x-ray procedures and the schools which train these individuals;
   (d) Develop, test, and promulgate high-yield patient referral criteria for diagnostic medical and dental x-ray procedures;
   (e) Review and approve or reject all existing and future Federally funded mass x-ray screening programs;
   (f) Develop minimum standards for State control of x-ray screening programs;
   (g) Develop and conduct programs to inform the public about the risks and benefits of medical radiation exposure;
   (h) Conduct studies to ascertain and recommend solutions to alleviate problems associated with overutilization of diagnostic x rays, e.g., malpractice; and,
   (i) Conduct studies to improve the timeliness, accuracy, and availability of radiologic diagnostic information, including the use of automated radiology scheduling and reporting systems.

2. Rationale: Misuse, non-use, or ineffectual use of compliant x-ray equipment can negate the objective of an equipment performance standard, and efforts of manufacturers to adequately design x-ray systems and components that meet the requirements of the standard. For example, authority to propose and enforce use/user standards would improve FDA's ability to increase safety factors in the operation of diagnostic x-ray machines where the safety factor is controlled by the operator.

B. Minimum State Standards Authority

1. Legislative Proposal: The Secretary shall be authorized to mandate and provide support for the adoption by States of minimum standards and regulations necessary to administer such standards, for the effective control of radiation; in the absence of State action, the Secretary is empowered to enforce the minimum standards in that State.

   Rationale: Such authority would allow for the Secretary to comprehensively address problems inherent with the total medical x-ray system by the establishment of minimum standards for State adoption with the prospect of Federal preemption should a State decline to adopt and enforce such Federally devised standards.

   Section 356 of P.L. 90-602 presently authorizes the Secretary to make grants to public agencies, such as State radiation control bodies, for the purpose of, among other reasons, supporting, planning, and conducting research, development, training, and operational activities; to study and evaluate conditions of exposure to electronic product radiation; and to develop, test, and evaluate such radiation protection programs.

   Section 360(e) currently authorizes the Secretary among other matters to reimburse the States for "any assistance in the administration and enforcement" of P.L. 90-602.

The Suggested State Regulations for the Control of Radiation conform to the requirement of Section 360(f) of P.L. 90-602, that State standards must be identical to the Federal standard with respect to the same aspect of performance of an electronic product that emits radiation.

This authority would expand the present authority and allow the Secretary to carry out more comprehensive radiation control programs, including the use of and inspection of diagnostic x-ray equipment within those States that either do not adopt and subsequently do not enforce minimum standards.

C. Research and Development Authority

1. Legislative Proposal: Expand Section 356 (a) (2) to specifically include the use of radiation used in the healing arts.

D. Radiation Source/Image Receptor Control Authority

1. Legislative Proposal:

   (a) Under Section 354, line 7, insert after the words "electronic products" the words, "including their safety and efficacy";
   (b) Under Section 355 (1), delete the words "electronic product"; and,
   (c) Under Section 358 (a) (1), line 3, insert after the word "products", the words "including all products or components used in the application of radiation in the healing arts, which affect the quantity, quality, and/or direction of such radiation" [7. b (4)].

2. Rationale: Section 358 states: "The Secretary shall by regulation prescribe performance standards for electronic products to control the emission of electronic product radiation from such products..." This is refined by the definitions in Section 355, and means essentially that these regulations can contain limits on the emission of electromagnetic, particulate, ~~and~~ acoustic radiation from products which have some electronic aspect to their nature. Nowhere does the Act distinguish electronic products intended for medical applications from other electronic products. The Act seems to have been written as if parasitic radiation emissions were the only radiation emissions of concern with no thought being given to useful radiation emissions, though no such distinction is made within the Act. We have written regulations which prescribe limits for useful radiation emissions with the thought that useful radiation emissions, which are more than actually required, are in fact unnecessary radiation emissions, and therefore, in some sense parasitic. This has never been challenged. The question before us is "How do we expand the scope of the authorities conferred on the Department by the Act in the most useful way?" There are several possibilities:

   (1) Expand the scope to include image receptors of electronic product radiation;
   (2) Expand the scope to include image receptors of electronic product radiation when such receptors are used in the practice of medicine;
   (3) Expand the scope to include all components of systems used in medicine for the diagnostic or therapeutic application of radiation, or in another form,
   (4) All products associated with the use of radiation in medicine.

   Number 4 is preferred.

A new definition could be added to Section 355 which would be a definition of the word "radiation". The definition would be the same as definition (1) with deletion of all references to electronic products. A new section could be added to the Act which would parallel Section 358 and confer the authority to prescribe by regulation performance standards for products associated with the use of radiation in medicine. This authority could be limited to the prescription of standards only for performance which is relevant to safety and efficacy of the radiation application or could be unlimited, and therefore, encompass all aspects of product performance. The latter approach may be unnecessarily duplicative of the authorities conferred by the Medical Device Amendments to the Food, Drug, and Cosmetic Act.

The fourth approach is preferred because in getting away from the term electronic product radiation, we can now deal with nuclear medicine, in removing the limitation of dealing with emission only we can now treat image receptors and protective devices and a minimum of modification to the rest of the Act is required. An alternative, would be to delete the definition of electronic product radiation; add the new definition of radiation; and then go completely through the Act, changing the term "electronic product radiation" to "radiation" wherever it occurs, and add the new section conferring authority to prescribe performance standards for all products associated with the use of radiation in medicine.

E. Pre-Operation Certification Authority

1. Legislative Proposal: Under Section 358 (h), insert the following new paragraph: "The requirements of the foregoing paragraph shall be applicable to newly installed equipment used in the healing arts, subsequent to its assembly and/or installation in a facility and prior to the initiation of its use in either diagnostic or therapeutic procedures".

2. Rationale: The present requirements for certification are given in Section 358 (h). This paragraph requires that manufacturers certify the compliance of products at time of delivery to distributors and dealers. This paragraph could be amended to require certification of products associated with the use of radiation in medicine at time of delivery (or transfer of custody) to a medical facility. There is a question here as to whether or not assemblers/installers of medical equipment should be specifically identified in the Act. The definition of "manufacturer" in Section 355 seems to cover the medical situation adequately, but there might be some usefulness in specifically identifying medical equipment assemblers. Here there is a question as to whether or not such identification in an amendment would imply that medical x-ray assemblers were not covered by the original Act.

   The question of certification (or recertification) by an assembler can be more effectively carried out by State health departments, assuming the availability of resources. If FDA directly administers this requirement, it means Agency involvement with the periodic testing of every piece of medical x-ray equipment throughout its useful life. That is a large responsibility, a large workload, and a large amount of information to manage - and costly. It would seem preferable to administer this provision under minimum standards for State programs and model legislation by stating to the effect: "State health departments shall require that medical facilities annually recertify compliance with applicable Federal performance standards for all products within their domain which are associated with the use of radiation in the healing arts." This would interface nicely with the warranty situation. Manufacturers who offered warranties longer than one year could, in their sales contracts, agree to assure that the equipment was in compliance at the time of annual recertification.

F. Seizure Authority

1. Legislative Proposal: The Secretary is authorized to seize noncompliant and/or defective products. Such authority should be employed where circumstances pose an immediate and significant risk of somatic or genetic injury to the general population.

   Such authority would cover all products still in commerce, i.e., those products not in the hands of consumers. X-ray machines in hospitals and doctors' offices would still be considered to be in commerce and, therefore, could be seized if they were defective or noncompliant. In order to accomplish this, it is proposed that Section 360C of the Act, 42 U.S. C. 263k, be amended by adding a new subsection (d) and renumbering the current subsections (d), (e), and (f), as (e), (f), and (g), respectively. Subsection (d) would read as follows:

   > (d) (1) Any electronic product, which is not in conformance with an applicable standard prescribed pursuant to Section 358 or which has a defect which relates to the safety of use of such product by reason of emission of electronic product radiation, when introduced into or while in interstate commerce or while held for sale (whether or not the first sale) after shipment in interstate commerce, shall be liable to be proceeded against while in interstate commerce, or at anytime thereafter, on libel of information and condemned in any district court in the United States within the jurisdiction of which the product is found.
   >
   > (2) The electronic product proceeded against shall be liable to seizure by process pursuant to the libel, and the procedure in cases under this section shall conform as nearly as may be, to the procedure in admiralty, except that on demand of either party, any issue of fact joined in any such case shall be tried by jury. When libel for condemnation proceedings under this subsection, involving the same claimant and the same issues are pending in two or more jurisdictions, such pending proceedings, upon application of the claimant seasonably made to the court of one such jurisdiction, shall be consolidated for trial by order of such court, and tried in (A) any district selected by the claimant where one of such proceedings is pending; or (B) a district agreed upon by stipulation between the parties. If an order for consolidation is so made within a reasonable time, the claimant may apply to the court one such jurisdiction, and such court (after giving the United States Attorney for such district reasonable notice and opportunity to be heard) shall by order, unless good cause to the contrary is shown, specify a district of reasonable proximity to the claimant's principal place of business, in which all such pending proceedings shall be consolidated for trial and tried. Such order of consolidation shall not apply so as to require the removal of any case, the date for trial of which has been fixed. The court granting such order shall give proper notification thereof to the other courts having jurisdiction of the cases thereby.
   >
   > (3) Any electronic product condemned under this section shall, after entry of the decree, be disposed of by destruction or sale as the court may, in accordance with the provisions of this section, direct and the proceeds thereof, if sold, less the legal costs, and charges, shall be paid into the Treasury of the U.S.; except that (A) such products shall not be sold under such decree contrary to the provisions of this subpart or the laws of the jurisdiction in which sold, and (b) after entry of the decree and upon the payment of costs of such proceedings and the execution of a good and sufficient bond conditioned that such product shall not be sold or disposed of contrary to the provisions of this

subpart or the laws of any state in which sold, the court may by order direct that such product be delivered to the owner thereof to be destroyed or brought into compliance with the provisions of this subpart under the supervision of an officer or employee duly designated by the Secretary, and the expenses of such supervision shall be paid by the person obtaining release of the product under bond.

(4) When a decree of condemnation is entered against a product, court costs and fees, and storage and other proper expenses, shall be awarded against the person, if any, intervening as claimant of the product.

(5) In the case of removal for trial of any case as provided by paragraph 2 --

> (A) The Clerk of the Court from which removal is made shall promptly transmit to the court in which the case is to be tried all records in the case necessary in order that such court may exercise jurisdiction, and (B) the court to which such case was removed shall have the powers and be subject to the duties, for purposes of such case, which the court from which removal was made would have had, or to which such court would have been subject, if such case had not been removed.

2. Rationale: At present, authority to seize can only be exercised under the Food, Drug, and Cosmetic Act, where medical equipment can be shown to be hazardous by virtue of radiation emissions or other electrical/mechanical hazards. However, seizure or "cease use" authority under P.L. 90-602 is needed to strengthen the Act with respect to noncompliant or defective electronic radiation-emitting devices.

G. Expansion of Prohibited Acts Section

1. Legislative Proposal: At the present time, the prohibited acts section of the Act, Section 360B (a) (1), provides that it is unlawful "for any manufacturer to introduce, or deliver for introduction into commerce, or to import in the United States, any electronic product which does not comply with an applicable standard prescribed pursuant to Section 358." This section should be amended as follows:

> (1) for any manufacturer to manufacture for sale, sell, offer for sale, introduce, or deliver for introduction into commerce or import into the United States any electronic product which does not comply with an applicable performance standard prescribed pursuant to Section 358 or which has a defect which relates to the safety of use of such product by reason of the emission of electronic product radiation.

H. Elimination of "Good Cause" Requirement for Inspections

1. Legislative Proposal: The Act should also be amended to eliminate the "good cause" requirement for inspections. As revised, Section 360A would read as follows:

> (a) For purposes of enforcement of this Subpart, officers or employees duly designated by the Secretary, upon presenting appropriate credentials and a written notice to the owner, operator, or person in charge, are authorized (1) to enter, at reasonable times, any factory, warehouse, establishment or vehicle in which electronic products are manufactured, tested, packaged, or held; and (2) to inspect, at reasonable times and within reasonable limits and in a reasonable manner, such factory, warehouse, establishment or vehicle and all electronic products and equipment, finished or unfinished materials, containers, labels, procedures and facilities which relate to electronic product radiation safety.

I. General Grant of Rulemaking Authority

1. Legislative Proposal: The Secretary is authorized to promulgate rules and regulations for the efficient enforcement of the Act.

2. Rationale: This type authority is contained in the Food, Drug, and Cosmetic Act: "Sec. 701(a). The authority of this Act, except as otherwise provided in this section, is hereby vested in the Secretary.

   Courts have consistently held that this provision authorizes the Secretary to issue substantive regulations. In other words, the regulations have the force of law, and a violation of the regulations is considered to be a violation of the law.

J. Technical Assistance Authority (including equipment calibration to parties not associated with Federal radiological health programs).

1. Legislative Proposal: Rather than adding to our management problems by adding a fee for service operation to our present operations, it might be more desirable to direct the Secretary to collaborate with the National Bureau of Standards in the establishment of regional calibration laboratories. This could be strengthened by requiring that instruments used in testing programs for certification of compliance with performance standards prescribed under the Act be calibrated annually or more frequently in regional calibration laboratories which have demonstrated adequate performance in a recent interaction with the National Bureau of Standards.

Mr. ROGERS. And could you give us FDA's assessment of Dr. Bross' and Dr. Bertell's finding from the Tri-State data which indicate increased leukemia incidence correlated with increased diagnostic X-ray exposure?

Dr. KENNEDY. Yes, sir.

Mr. ROGERS. Maybe you could give us quickly your reaction to these findings. Do you feel they are legitimate?

Dr. KENNEDY. I think I would like to ask Mr. Villforth to do that as well, because I think he is more familiar with them than I.

Mr. ROGERS. Certainly.

Mr. VILLFORTH. I think the simple answer to this type of project, that is the Tri-State project, or to the Mancuso work at Stanford or to the Najarian study at New Hampshire is these studies must be reviewed; they must have the opportunity to be given scientific test in the open literature, and when we have a chance to review the reviews and the initial reports, we will be in a better position to draw judgments. I think there are merits in all of these studies. There are also some problems and concerns we have with all of these studies.

I would like to point out, as an illustration, the original Mancuso paper was published in the Health Physics Journal. There are two rebuttal articles to that paper. One is published in the June issue of the Journal, which has not been distributed yet, and another rebuttal is accepted for publication and will be scheduled shortly.

The concern I have is that the scientific community needs to have the benefit of the original articles, the rebuttal articles and the dialog that is going to take place for some time, for months hereafter to give an informed judgment. I don't feel that I have enough information to know which way things are going to go.

[The following information was received for the record:]

AN FDA ASSESSMENT OF THE BROSS AND BERTELL WORK

The FDA's Bureau of Radiological Health staff are familiar with the work of Dr. Bross on the Tri-State Leukemia Study, since it studies similar subject matter as the work of Dr. Stewart on the Oxford Survey of Childhood Cancer, which is funded by the Bureau. Because of the existence of biasing factors in epidemiologic studies, it is necessary to seek corroboration of observed effects from two or more independent studies. BRH staff has found that the Bross work and the Stewart work agree in the basic finding of an approximate 50% increase in the risk of leukemia following in-utero irradiation and of an increased sensitivity to certain childhood diseases among leukemia victims.

The findings of an association between preconception irradiation and increased risk of leukemia was initially found in both studies. An in depth sophisticated analysis of this effect by Dr. Stewart, however, has indicated that this association is more likely an artifact of the reporting of the timing of the x-ray examinations rather than an effect of radiation.

With regard to the most recent work of Dr. Bross, purporting to show a genetic link between in-utero irradiation and cancer, we feel that neither the data nor the mathematical methods are sufficient to test such a precise hypothesis. This work was recently reviewed by Dr. Kenneth Rothman in a public meeting given by NRC at the request of Dr. Bross. In that review Dr. Rothman accurately critiqued the most recent Bross work as circular logic in the sense that Dr. Bross is using his data to formulate a hypothesis and using the same data to "prove" the hypothesis. This type of approach is not legitimate because it violates the scientific method.

Another review of the paper in the Journal of the American Medical Association was given by Dr. Charles Land in a Letter to the Editor of that Journal. In that review, Dr. Land showed that the model put forth in the paper could better fit the data if estimates other than the ones Dr. Bross used were employed. Dr. Bross implied in a reply that his estimates were "good enough" but such a response violates the statistical principle employed by Bross, i.e., minimum chi-square estimation. If another set of estimates produces a smaller chi-square, one must continue to search until the global minimum is attained.

Furthermore, the Bross model purports to test a genetic hypothesis without having direct observation of a genetic result. Any number of mechanisms (genetic or other) could be used to explain the observed results. Thus, we feel that Dr. Bross has not shown in this more recent line of research that which he has purported to show.

With regard to the analysis by Dr. Bertell, the method appears to hypothesize that the only effect of radiation is an aging effect such that an increase in leukemia risk in an exposed population can be totally explained by a simple linear shift in the biological age of the exposed individual. Dr. Bertell proposes to test this hypothesis by estimating the rate constant (increase in age per rad skin exposure), by adjusting the age cohorts in a small segment of the Tri-State Leukemia Study to account for the radiation, by calculating a new summary relative risk across these cohorts, and by calculating a chi-square value associated with the new relative risk value. The final estimate is achieved when the new relative risk reaches unity.

Yet, Dr. Bertell presents an apparent estimation method as though it were a hypothesis testing method. In statistics these two aspects of inference are related but are distinct. Even, if one were to accept the hypothesis, the implications would be only that the association between radiation and leukemia risk is not dissimilar from the association between age and leukemia risk. The mechanisms for these two associations may be quite different.

Dr. Bertell utilizes her results as though she has proven a cause-effect type of relationship; i.e., radiation causes a biological aging with respect to leukemia sensitivity. In fact all she has done is to find an estimated value for the rate constant of an assumed age-radiation dose relationship which best fits the Tri-State Leukemia Study data. The latter demonstration is necessary for the former proof but is by no means sufficient.

Mr. ROGERS. What inspection do you do in California, or do you leave that mainly to the State?

Mr. VILLFORTH. The California program in terms of the X-ray, as far as I know, California is one our contract States, just like the other 22.

Mr. ROGERS. You have 22 States that you contract?

Mr. VILLFORTH. Contract States.

Mr. ROGERS. They do the inspection for you.

Mr. VILLFORTH. For new equipment that is installed, the assemblers assembled equipment. As the Commissioner said, we put in an additional $400,000 to add to these 22 States and hope to get another 20 or so States on top of that, which will help to a large extent, or maybe double the number of compliant inspections of new equipment.

Mr. ROGERS. In the contract do you have certain standards? For instance, for an X-ray machine, standards for at what point it should be closed down?

Mr. VILLFORTH. We have a specific protocol that they are to follow, including the type of testing, the way it is to be tested, because we must have consistency from State to State. We provide the instrumentation.

For example, when we receive from the Food and Drug Administration an additional $400,000 to contract for these additional States, to increase the 22 we had to go back to our friends in the Food and Drug Administration and ask for $168,000 more for new equipment to support those contract States. So we have bought the equipment.

We have trained the State people to do this, and there is a specific protocol.

Mr. ROGERS. How often are you asking that the machines be checked by the States in your contract with them?

Mr. VILLFORTH. This is not a case of how often. We are asking them to get a certain percent of the new machines installed that year, which means some machines won't get inspected that year.

Mr. ROGERS. Are you doing any reinspection of old equipment at all?

Mr. VILLFORTH. To my knowledge, there is no routine inspection of old equipment under this protocol by us under the contract.

Mr. ROGERS. What about new equipment; is there a routine set for inspection, reinspection?

Mr. VILLFORTH. I have just been informed that up to 10 percent are reinspected by the States. The contract with the States allows for about 10 percent of the machines to be reinspected.

Mr. ROGERS. California, I think, which has 10, 12 percent of the medical and dental X-rays, advises that dental equipment is checked on an average of once every 20 years, and priority machines, that is the ones in high-use areas such as hospitals, are only checked every 4 years. Is that a reasonable inspection program?

Mr. VILLFORTH. It does not appear to be a reasonable inspection program.

Mr. ROGERS. Would you let us know what is a reasonable inspection program and what action we should take and the probable estimates of costs if we got into something like that?

[The following information was received for the record:]

REASONABLE STATE X-RAY EQUIPMENT INSPECTION PROGRAM

A reasonable inspection program for medical and dental diagnostic x-ray facilities should provide for the inspection of the x-ray equipment itself, and, more broadly, inspection of the x-ray facility with regards to its radiation protection and quality assurance activities. Inspection of x-ray equipment should include the testing of: (1) newly installed certified systems and components; (2) certified equipment that has been in use for an extended period of time in order to assure continued compliance; and, (3) equipment manufactured prior to the 1974 FDA standard. Inspection of the facility should include review of: (1) the facility's awareness and implementation of quality assurance and good practice recommendations; and, (2) compliance with State recommendations and regulations for patient and personnel protection.

Currently, inspections of x-ray equipment by FDA and by State radiation control agencies under contract with FDA are concentrated on newly certified systems. Until the noncompliance rate is reduced, the FDA inspection program should provide for the testing of 100% of newly installed general purpose units (equipment that is totally assembled at the final facility), 30% of mobile x-ray units, and 10% of dental x-ray systems within the first year following installation. Also, up to 10% of the certified equipment is reinspected annually by the States. We believe that these goals will provide us with sufficient data to detect the noncompliances caused by the design, production, or assembly of the components and systems manufactured under the diagnostic x-ray standard.

Although the routine inspection (and reinspection) of x-ray equipment/facilities has traditionally been the responsibility of the States, both FDA and the States have given continued attention to updating criteria for "reasonable" inspection programs. In the past, primary emphasis has been placed on equipment inspections alone; however, there has been a growing awareness that an effective inspection program must also serve to educate and/or regulate x-ray facilities with regards to quality assurance and good practice activities.

New developments in this regard are resulting from FDA involvement with task forces of the Conference of Radiation Control Program Directors. One task force has tentatively proposed the following inspection schedule as a guide for State agencies:

(a) dental x-ray machines - every 5 years;
(b) hospital or similar facility - every year;
(c) clinic (radiologist) - every year;
(d) chiropractor - every year;
(e) osteopath - every 2 years;
(f) medical x-ray machines (other than those listed above) - every 2 years; and,
(g) veterinarians - every 2 years.

Other task forces on Suggested State Regulations, BENT, and on Quality Assurance are providing models, goals, and specific action programs that States can use to improve their inspection programs.

One current estimate of the manpower required to implement a reasonable x-ray inspection program, as described above, is three full-time equivalents for every 1000 x-ray tubes. This would result in an approximately 400% increase in funds and personnel over what is currently being spent.

Dr. KENNEDY. I think, Mr. Chairman—if I might be permitted an observation—that is going to turn out to be very difficult. Like anything else, there is a rather complicated cost benefit ratio that applies to the application of resources and probable varying rates of return as one moves up the curve.

We believe that although our sampling rate is not high, that we are getting a good-sized piece of the problem. The choice is likely to be, if you take a marginal $100, do you invest it in educational work with providers and consumers to reduce the numbers of unneeded exposures, or do you invest it in compliance and inspection programs for equipment, and which one gives you the largest rate of return?

It is very tough to know. Our best guess is that we will be spending our dollars a little better if we spend them on reducing unneeded exposures as opposed to increasing our sampling rate of equipment that we inspect. It is going to be a tough call.

Mr. ROGERS. I wonder why it couldn't be carried out rather inexpensively if a concerted effort is made to call your professional people together to discuss this problem and really put on a concentrated program to get across this type of information I feel that they would not resist an educational program, but it may have to be initiated by us in a very dramatic way. It seems to me the Commissioner of Food and Drugs could call together the leadership from the States, maybe the major cities of the country and the hierarchy of the various colleges and the AMA to get across these points that really ought to be handled by the profession. We shouldn't have to educate the public to tell a doctor that they don't want something that the doctor knows ought not to be good for them.

It seems to me that that is kind of a back-door approach. I understand there is some problem with such an education program, but I think a more active effort could perhaps accomplish it.

Dr. KENNEDY. But I do think, Mr. Chairman, that it is fair to say that we are moving effectively through the front door as well as the back door. But assembling the medical profession in one place to hear pronouncements from this particular part of their government is not as easy as it can be made to sound.

Mr. ROGERS. Well, nothing is easy, Mr. Commissioner, but I think you would be surprised at the results you would get if you would call. And I think Members of the Congress would be helpful, I think the Secretary would be helpful, I expect the Administration would be helpful in convening State officials, health people, the colleges to a conference to discuss some of these very serious matters that they would prefer to avoid the need for Federal regulations on.

In other words, why can't you activate the doctors to do it themselves? I think we could, rather than doing all the studies—when we already know there is a problem. We already know you are ready to put out information to tell the women who read the sign, don't let your doctor zap you there with that X-ray. Now we ought to be able to get this information to enough of the leadership of the medical profession, and this committee would help you to get that done.

Dr. **Kennedy**. Mr. Chairman, I am convinced you have created, obviously, with these hearings a very intense public interest in the problem, and I think perhaps created the conditions under which exactly the sort of program you suggest will be helpful. We will go to work on it and come back to you with some proposals, and I expect you will be asked to participate in it.

Mr. **Rogers**. The committee would be willing to work with you. In fact, I think we ought to do more of this, and I think if we could have key people in each State that could alert people to get these messages across to the profession, every State, every city—they have the organization to do this—it could be done.

This committee, I am sure, would be glad to work with you in any way it could.

Dr. **Kennedy**. That is splendid, Mr. Chairman. We will be back to you promptly for a proposal on that.

Mr. **Rogers**. There may be other questions we may ask for the record. You have been with the committee for so long.

Thank you very much, Mr. Commissioner, and we hope the materials asked for will be furnished as soon as possible. Thank you for your presence today.

Our last witness will be from the the American College of Radiology, Dr. Russell H. Morgan, University Professor of Medicine, the Johns Hopkins University School of Medicine, Johns Hopkins Hospital; and Dr. Harold O. Wyckoff, president of the International Commission on Radiation Units and Measurements and will be accompanied by Otha Linton, who is Director of Governmental Relations, the American College of Radiology.

We welcome each of you to the committee. We apologize to each of you for holding you here too long this afternoon, but it is good to see you again and we are grateful for your presence.

Your statements will be made a part of the record, and if you could summarize the highlights for us, it would be most helpful.

STATEMENT OF RUSSELL H. MORGAN, M.D., ON BEHALF OF AMERICAN COLLEGE OF RADIOLOGY, ACCOMPANIED BY HAROLD O. WYCKOFF, PH. D., PRESIDENT, INTERNATIONAL COMMISSION ON RADIATION UNITS AND MEASUREMENTS, AND OTHA W. LINTON M.S.J., DIRECTOR OF GOVERNMENT RELATIONS

Dr. **Morgan**. Thank you.

I am Dr. Morgan. On my left is Dr. Wyckoff, and on my right is Mr. Linton.

Before beginning my testimony, I would just like to digress for a moment to make one comment. On the basis of your recent announcement, Mr. Chairman, this is most likely to be the last opportunity that we will have for discussion of this sort with you. I want to express for all of us in the profession, and particularly for those of us in the specialty of radiology, our heartfelt thanks for the wonderful and magnificent job you have done through the years. I speak with the deepest sincerity. We shall miss you very much.

Mr. **Rogers**. That is very kind.

Dr. **Morgan**. Because the hour is late, let me just summarize things very quickly.

Our testimony, of course, is offered on behalf of the 12,000 radiologist and physicist members of the College of Radiology. About 90 percent of the Nation's medical specialists in the uses of ionizing radiation and other energy forms for diagnoses and treatment of disease are members of the College. Several hundred radiological physicists are also members.

We are pleased to respond to your committee's request for an assessment of the current status of the medical uses of radiation as well as to make comments on several matters of concern to us and to the subcommittee.

Our testimony consists of a brief introduction and then several sections outlining areas of background comment requested by the subcommittee and some observations and comments upon current Federal programs.

Unless the subcommittee prefers otherwise—and I presume that because the hour is late this will not be the case—we propose merely to read the introduction and perhaps a little of the discussion.

Mr. ROGERS. Certainly. I think that will be fine where you highlight the points for us.

Dr. MORGAN. This is not the first time that we have testified, of course, before this subcommittee. We were pleased to contribute to your deliberations which led to the enactment of Public Law 90-602 in 1968. From the vantage point of 10 years, we think the law has been a reasonable and workable one. Taken on the whole, it has been reasonably and soundly implemented in a manner which supports its intention; namely, the protection of the American people from injuries associated with exposures to ionizing radiation in several contexts.

Just 50 years ago, radiologists persuaded the Federal Department of Commerce to assign one scientist within the Bureau of Standards to the field of ionizing radiation. That scientist, Dr. Lauriston S. Taylor, who I am sure is known to everyone in the room, has spent a distinguished career in radiation science and has seen himself succeeded by several thousand scientists and administrators in a growing array of Federal agencies. Some of the current burden of this Federal attention is outlined in the article by Moseley and Linton, which is attached to our testimony. [See p. 531.]

During the same half century, radiology organizations have accepted responsibilities for radiation safety of X-rays and radioactive materials used in medicine. They have been principal sponsors of the National Council on Radiation Protection and Measurement and its predecesor organizations. They have contributed to the workings of several international radiation study groups. They have contributed, as outlined elsewhere, to the enactment of legislation at the Federal and State levels, to the creation of Federal and State agencies which have broad responsibilities to support appropriate and effective uses of ionizing radiation as well as the regulation of radiation equipment.

Two decades ago, when I and 10 or 12 of my colleagues, who then constituted the National Advisory Committee on Radiation, began calling the public's attention to the need for Federal regulation of ionizing radiation—medical and otherwise—we often wished that we could attract more attention by the public and by the Government. Now, 20 years later, we sometimes think we may have perhaps overdone it.

Last June, the College testified before your colleagues on the Senate Commerce Committee in its oversight hearings. In the course of those hearings we cited three ways in which we are presently distressed about Federal programs. A year later, we think the same three problems exist. In brief, they are:

One, an absence of a focus—I did say focus, but I think one needs to say a highly competent focus for radiation-related research within the Federal Government.

Mr. ROGERS. May I just interrupt there?

Dr. MORGAN. Yes.

Mr. ROGERS. Would you feel the main thrust of that research should be in the health agency?

Dr. MORGAN. Yes, indeed; because the problems are health related. It is as simple as that.

Mr. ROGERS. Thank you, Doctor.

Dr. MORGAN. It doesn't require any complicated philosophical approach.

Mr. ROGERS. Thank you.

Dr. MORGAN. Two, an overlapping and sometimes contradictory pattern of regulatory efforts by Federal and State agencies in the health field and elsewhere in government is another problem that we see.

And three, an undue emphasis on health-cost containment, which seems likely to stifle further development in radiation equipment and its application, which worries us, not because there need not be concern here, but because I see some evidence that if we are not careful we may go too far in the direction of cost containment, to the disadvantage of the people of the Nation who need health care in the future.

So these three things, Mr. Chairman, are problems which we see, and I, as well as Dr. Wyckoff and Mr. Linton, would be glad to answer questions now regarding them.

[Testimony resumes on p. 534.]

[The prepared statement of Drs. Morgan, Wyckoff, and Linton, and attachment follows:]

STATEMENT

for

Subcommittee on Health and Environment
Committee on Interstate and Foriegn Commerce

on behalf of

The American College of Radiology

Russell H. Morgan M.D.
Harold O. Wyckoff Ph.D.
Otha W. Linton, M.S.J.

12 July, 1978

Mr. Chairman, thank you for this opportunity to share our comments.

I am Dr. Russell H. Morgan of Baltimore. I am a university professor of medicine at the Johns Hopkins University School of Medicine. I was formerly chairman of radiology, dean of medicine and vice chancellor of medical affairs at Hopkins. I am accompanied by Dr. Harold O. Wyckoff, a distinguished physicist now retired from the National Bureau of Standarc and the Department of Defense who is president of the International Commission on Radiation Units and Measurements, and by Mr. Otha W. Linton, director of government relations for the College.

Our testimony is offered on behalf of the 12,000 radiologist and physicist members of the American College of Radiology. About 90 percent of the nation's medical specialists in the uses of ionizing radiation and other energy forms for diagnosis and treatment of disease are members of the College. Several hundred radiological physicists also are members. We are pleased to respond to your committee's request for an assessment of the current status of medical radiation uses as well as making comments on several matters of concern to us and to the subcommittee.

Our testimony consists of a brief introduction, several sections outlining areas of background comment requested by the subcommittee and some observations and comments upon current federal programs. Unless the subcommittee prefers otherwise, we propose to read the introduction and the discussion of current programs and to request that the other portions be entered into the record.

This is not the first time the College has testified before this subcommittee.

We were pleased to contribute to your deliberations which led to enactment of Public Law 90-602 in 1968. From the vantage point of 10 years, we think that has been a reasonable and workable law. Taken on the whole, it has been reasonably and soundly implemented in a manner which supports its intention--the protection of the American people from injuries associated with exposures to ionizing radiation in several contexts.

Just 50 years ago, radiologists persuaded the federal Department of Commerce to assign one scientist within the Bureau of Standards to the field of ionizing radiation. That scientist, Dr. Lauriston S. Taylor, has spent a distinguished career in radiation science and has seen himself succeeded by several thousand scientists and administrators in a growing array of federal agencies. Some of the current burden of this federal attention is outlined in the article by Moseley and Linton which is attached to our testimony (enclosure 1).

During the same half century, radiology organizations have accepted responsibilities for radiation safety of x-rays and radioactive materials used in medicine. They have been principal sponsors of the National Council on Radiation Protection and Measurement (NCRP) and its predecessor organizations. They have contributed to the workings of the several international radiation study groups. They have contributed, as outlined elsewhere, to the enactment of legislation at the federal and state levels, to the creation of federal and state agencies which have broad responsibilities to support appropriate and effective uses of ionizing radiation as well as the regulation of radiation equipment.

Two decades ago, we sometimes wished that we could attract more federal attention to problems of medical radiation control and applications. Now we sometimes think we or somebody has overdone it. Last June, the College testified before your colleagues on the Senate Commerce Committee in its oversight hearings. In the course of that hearing, we cited three ways in which we are presently distressed about federal programs. A year later, we think the same three problems exist. In brief, they are:

1. Absence of a focus for radiation-related research within the federal government.
2. An overlapping and sometimes contradictory pattern of regulatory efforts by federal and state agencies in the health field and elsewhere in government.
3. An emphasis on health cost containment which seems likely to stifle further development in radiation equipment.

II Status and extent of medical radiology in United States.

The late Dr. R. H. Chamberlain estimated that perhaps a third of all significant medical decisions are influenced strongly by the information obtained in a diagnostic x-ray examination. If we extrapolate from the 1970 X-ray Exposure Survey made by the Bureau of Radiological Health, we might assert that seven of every ten Americans receive some medical radiation procedure in any given year. An overwhelming portion of those procedures involve diagnostic x-ray examinations. A smaller number involve procedures to study motion, termed fleuroscopy or special procedures. The special procedures are those in which liquids opaque to x-rays are injected into the blood circulatory system.

A smaller number, perhaps two million or less, receive high-energy radiation treatment for diseases, principally cancers.

Perhaps eight to ten million persons receive examinations using radioisotopes yearly. Others are examined using ultrasonic energy or thermal energy. The rapid growth of these modalities has prevented any specific estimates of their totals.

Data from the 1970 PHS x-ray survey suggests that some 64 percent of medical x-ray procedures are performed in hospital x-ray departments. Almost all of these are the responsibility of radiologists. Of the remaining 36 percent, the PHS estimated that one fifth were performed by radiologists in offices and clinics. The remainder were performed by other physicians and limited practitioners whose licensure allows the use of x-rays. In general terms, Then, it might be presumed that specialists in radiology perform two-thirds of all medical radiation procedures.

A recent study by the American Society of Internal Medicine indicated that 48 percent of internists own x-ray equipment. W.thin the same group of respondents, 6 percent performed nuclear medicine examinations and 19 percent essayed fluoroscopic examinations, normally using greater radiation exposures than radiographic examinations.

Since the use of x-rays is historically included as part of medical licensure in most states for physicians and for limited practitioners such as podiatrists or even chiropractors, there is no legal inhibition upon such uses, even though questions have been raised in recent years about training and qualifications. Only California, of all the states, requires licensed health practitioners to attest to competence in x-ray use.

Over the past decade, recruitment into radiology has nearly tripled the ranks of specialists. Including those now in residency training, the American Medical Association reflects some 16,000 physicians claiming specialization in one of the branches of radiology (diagnostic radiology, radiation therapy or nuclear medicine) which are credentialed by the American Board of Radiology. (ABR) These radiologists have completed a three-year residency program and have passed the ABR examination.

This increase in numbers has been studied by the ACR in three studies. (enclosures 2, 3 and 4) Such studies have indicated that the manpower supply in radiology is now adequate and is sufficiently well distributed to undertake the radiologic procedures now required by Americans. However, if other physicians are restricted in their uses of x-rays and if the current emphasis upon primary care physicians creates an increased demand, then current recruitment and training levels may not remain adequate for the 1980s.

Radiologists are supported in their work by radiologic physicists, radiobiologists, statisticians and other scientists. In particular, they are aided in procedures by more than 100,000 persons who are termed radiologic technologists or radiographers. An additional estimated 40,000 to 70,000 persons are believed to be employed as x-ray operators without benefit of formal training or credentials. The 100,000 technologists are those who have completed training programs and who have passed voluntary examinations of the American Registry of Radiologic Technologists.

Radiologists are also supported by a variety of manufacturers of equipment and supplies. Sales to the American Medical x-ray market were estimated by the National Electric Manufacturers Association (NEMA) to be approximately $600 million in 1976. The costs of x-ray equipment have reflected the general rate of inflation plus added costs incurred incompliance with requirements under PL 90-602 and more recently PL 94-249, the medical device act.

The addition of a positive beam limiting device on general purpose radiographic systems has been estimated to add from $1500 to $6000 to the cost of the unit. It is too early to be able to estimate clearly the costs of complying with regulations to be implemented by the Food and Drug Administration under the medical device law.

In the past five years, the most obvious impact upon the x-ray market has been the advent of the computerized tomographic scanner. This is a remarkable advance in medical technology which enables radiologists to make precise and safe studies of most body parts and organ systems. The combination of an x-ray gantry with a computer to analyze several thousand signals and create a transverse or cross-sectional image has required both mechanical and electronic innovation. Scanners capable of examining most body parts range in initial cost from $350,000 to $650,000. NEMA recently announced that at the end of 1977, some 921 CT scanners were operating in the U.S. with an unspecified number on order or awaiting installation.

Quantitatively, the number of CT scans is hardly comparable with the 130 million x-ray procedures performed yearly. However, a combination of factors appears to have had a definite retarding effect upon the growth of x-ray services. Anecdotally, radiologists and manufacturers have reflected a flattening or even a down-turn of the growth curve in radiology beginning in 1976. Whether this reflects the impact of inflation, the impact of quality assurance programs, the impact of professional standard review, the impact of radiation scares or all of the above and still others remains speculative.

Though the ACR does not attempt to be a center of research or of records, the College does conduct various studies from time to time. It also maintains a vigorous liaison program with the x-ray industry and with state and federal agencies having responsibilities for radiation uses. As noted above, the College and other radiology groups have sponsored and participated in activities of the NCRP since its inception.

All this activity by physicians using radiation results in an average annual exposure to Americans of 60 to 100 milliroentgens according to NCRP estimates. This range is given because the values differ for various organs and tissues. Roentgens, rads and rems are units which describe the amount of radiation involved. The number of roentgens gives a measure of the photons involved. The number of rads and rems describe a radiation dose absorbed at some point within a living creature or test object. Depending upon the density and atomic composition of the creature or object, the absorbed dose in rads is some fraction of the exposure in roentgens. A millirad is 0.001 parts of a rad.

The average medical exposure is less than a tenth of a roentgen. This compares to the average annual exposure from background or natural radiation of 80 milliroentgens. This background radiation consists of cosmic rays from the sun and stars plus the emanations from naturally occurring radioactive elements in building materials, the soil, water and even air. The amount added by man-made sources other than those used in medicine is inconsequential in terms of average national exposures. However, occupational and environmental exposures can be most significant to persons who work with radiation in medicine, electric power generation, industrial testing and military applications.

Members of this subcommittee will remember that a major impetus for passage of PL 90-602 in 1968 was a concern for x-ray exposures from color television sets and other consumer products.

AS NCI director Dr. Arthur C. Upton, a distinguished radiation scientist, told the subcommittee in February, there are three types of concern about radiation exposure. One is the genetic risk. This risk involves the thousands or millions of extremely small exposures which may be essentially harmless to the individuals receiving them but which cumulatively may affect the total genetic pool of the population. The second is the teratogenic risk that radiation exposures of a fetus may cause pre-natal death, developmental anomalies or an abnormal tendency toward cancer induction later in life.

The third is the direct somatic effect upon the person receiving the exposure which may harm him at the time of exposure or which may predispose him to disease later in life.

Questions about how much radiation can be tolerated safely by whom, what levels of exposure are acceptable for the public and for various groups within the public and what kinds of public sanctions, if any, are required on radiation uses, will be discussed later herein, as they have been before the subcommittee by other witnesses.

The general rule for medical exposures is that anticipated benefits should clearly outweigh potential or inherent risks. Such benefits would include contributions to a diagnosis or the impact of radiation upon a radiation-responsive disease, such as cancer. In any instance, the physician is adjured to use the minimum amount of radiation needed to accomplish h's purpose, to use "as little as practicable".

III Purposes and methods of medical radiology.

Patients are exposed to ionizing or other forms of high energy radiation for one of two reasons. The overwhelming proportion of the time, the intent is to gain diagnostic information. A small but critical proportion of these exposures are for the treatment of disease, principally cancer.

When ionizing radiation is used for treatment, the intent is to administer a dose of radiation which will destroy diseased tissues. Such doses range from several hundreds to several thousands of rads. Exposure of the whole body to such doses, either in a single sitting, or in a series of sittings is likely to be lethal. The challenge to the radiotherapist is to devise treatment systems whereby a lethal dose of radiation is delivered to the cancer while surrounding normal tissue is spared, thus avoiding unacceptable side effects to the patient.

A physician treating cancer can choose among surgery, chemicals, hormones and radiation, according to the tumor site, cell type, extent, invasiveness and other factors. Often a combination of treatments is chosen. Those cancers chosen for radiation are of cell types which are known to be responsive to radiation, thus allowing a "therapeutic ratio" of destruction of cancer cells while sparing normal tissue.

In the instance of a cancer patient, the inexorable progress of untreated or unsuccessfully treated disease makes the level of risk from massive radiation or other traumatic treatments a necessary and tolerable choice. Some kinds of cancers are treated successfully by radiation and the patients so treated live normal lifespans subsequently. Indeed, some women have borne normal children following radiation treatments involving several thousands of rads close to their reproductive organs.

The larger numbers of people exposed to radiation are for diagnosis, detection and identification of disease as reflected in anatomic or functional deviations from the normal. The greatest proportion of such examinations produce static x-ray images of various body structures and do not involve the ingestion or injection of contrast materials. If motion is of concern the x-ray images can be supplemented or replaced by fluoroscopic exposures.

In fluoroscopy, the x-ray beam is directed through a patient while the radiologist observes anatomic movement in "real time". To study the upper gastro-intestinal system, the patient is asked to swallow a barium sulphate mixture, opaque to x-rays, which the radiologist watches traverse the pharynx and esophagus into the stomach. The exposures required for fluoroscopy are higher than those needed for static x-rays. However, the use since the late 1940's of electronic equipment enhancing the x-ray signal makes possible clear images with exposure levels that physicians believe to be quite safe.

Some types of examinations, special procedures, may involve the insertion of hollow catheters into blood vessels and the injection of contrast materials into them for the study of the heart, brain, kidneys or other organs. Such procedures may be recorded on motion pictures, film or videotape, as well as being monitored during performance.

Radioactive materials can be used for diagnostic imaging. Normally, a radioisotope such as technetium 99m, is chemically bonded to a substance which seeks certain body organs or tissues. To study the thyroid, for example, an iodine based compound would be chosen. The radioactive material is injected into the patient and allowed to pool in the organ to be studied. A sensitive detector is then positioned over the organ and the emitted radiation is recorded. Abnormal patterns in the concentration of the radiation can be interpreted by radiologists to make a diagnosis.

Ultrasonic devices also are used to make diagnostic images. The pulsed diagnostic ultrasound is used in several modes to reflect signals from internal body structures thereby producing a pattern which a skilled radiologist can interpret.

The images produced by ultrasound or radioisotopes lack the fine detail achievable on x-ray studies. But they have advantages for the study of organs which are difficult or impossible to image effectively by x-ray methods.

The newest development in medical x-ray imaging is the computed tomographic (CT) scanner. This sophisticated machine combines the x-ray and a computer to generate unique cross-sectional images of the human body which are enormously valuable in the diognosis of disease.

The conventional x-ray or fluoroscopic system views the body from a fixed perspective. An x-ray beam passed through the chest from back to front, for example, is absorbed in part by the ribs and other body structures. The images generated by the various structures of the chest are superimposed on one another on the x-ray film.

The CT scanner creates a transverse or cross-sectional image of a selected body section by rotating the x-ray source and image receptor around the body by mechanical and electronic means. Many thousands of separate bits of information are generated and a computer program arranges this information into an image in which each organ or structure stands out.

CT scanning was accepted instantly and enthusiastically by radiologists for a variety of examinations because of the superiority of the information obtainable and the substantial savings in time and trauma to patients. The special procedures in which contrast media are injected into the brain or other organs involve some risk and substantially more time than do CT examinations. T scanning will not replace all special procedures but it is already resulting in reductions of many, particularly the complex and painful pneumoencephalograms used heretofore to study the brain.

Health planners and health insurors have expressed concern about the proliferation of CT scanners because of their relatively high initial cost and operating expense. Answers for all of these concerns is beyond the scope of this testimony. However, it is worth noting that the radiation exposures for CT examinations are comparable to those involved in special procedures and the information they provide is remarkably better. The day is not far away when the CT scanner must be considered an essential instrument for all hospitals offering full diagnostic radiologic services.

A brief description of the basic physical principles which are applied in medical use of radiation may be helpful for understanding the importance of such radiation in medical diagnosis and treatment.

Photography is the process in which light reflections are recorded on sensitive film. Radiography is the process in which ionizing radiation is projected through an object differentially absorbed by the structures within it and then recorded on film or a fluoroscopic screen.

To use the chest film as an example, the x-ray energy differentiates among four tissues, bone, water, fat and air. On the x-ray film, bones show up as white, meaning that the calcium in them has blocked most of the x-ray photons impinging upon them. The densities of water and fat are reflected in subtle shades of gray. The air in the lungs blocks less radiation and thus where there is air the film is blackened to the greatest extent. The radiologist's task is to analyze the overlapping pattern of shadows to detect variations from normal.

The various components of the x-ray system must be coordinated to produce films of good diagnostic quality. Current technology recommends the use of relatively high energies, 60 to 125 kilovolts, and short exposure times, a tenth to a thirtieth of a second, for chest examinations. The response characteristics of x-ray films and of the associated intensifying screens (which enhance the sensitivity of the film) are carefully matched to the x-ray beam for optimal diagnostic results. Even modest variations result in a loss of detail in the lung fields.

In general, the amount of diagnostic information recorded in an x-ray film varies inversely with the radiation dose delivered to the patient. Because the acquisition of diagnostic information is the basic reason for performing radiographic examinations and because radiation exposure may pose some risk, every radiographic examination requires the physician and his radiologist colleague to balance clinical benefit against possible risk. Overemphasis on the risk will cause the needed diagnostic information to fall short. Diagnostic information beyond that required, may cause patients to be exposed to unnecessary risk. Fortunately, the risks of radiography with current radiation levels are vanishingly small and overemphasis on the risk problem must be a much greater concern for society than overemphasis on diagnostic information.

In this connection, it must be pointed out that there is a constant effort by radiologists, manufacturers and regulators to improve the efficiency of the radiographic process to reduce as far as possible the radiation dose delivered to patients. As an example, recent developments in special films for mammography by leading manufacturers have allowed a significant reduction in the average exposure and dose from that procedure without loss of critical information.

Most of the technical developments in radiologic imaging have come from cooperation between radiologists and the companies which make x-ray equipment and supplies. Phototiming which automatically matches exposure characteristics to the patient's size, was devised by a radiologist, Dr. Russell H. Morgan, and made available to the industry. Dr. Morgan later contributed to the development of electronic image intensification which makes possible modern fluoroscopy by amplifying a weak radiation signal a thousand-fold or more to permit viewing fluoroscopic images in natural light or recording them on movie film or television tape.

In the past decade, many innovations in radiology have resulted from the availability of engineers formerly employed in various space programs. The solutions to problems of transmitting and reproducing an image of the surface of the moon are applicable to reproducing and transmitting images of the kidney or pituitary gland.

Since the promulgation of the performance regulations for x-ray systems by the Bureau of Radiological Health in 1974, the requirements for beam limitation and consistency of beam production have reduced radiation exposure without loss of diagnostic information.

Much of the development of nuclear medicine procedures is directly dependent upon the sponsorship of research and development by the Atomic Energy Commission and its successor agencies. The whole family of short-lived radioisotopes applicable to medical uses and the development of the gamma camera for recording the distribution of these materials in the body should be credited to AEC funding and related support.

Most of the work on ultrasound is again a product of collaboration between the medical profession and industry with a limited impetus from the National Science Foundation, mostly at the clinical application level. Almost no federal effort has gone into development of the CT scanner. Such development took place first in England by the EMI Corporation and subsequently in this country by a dozen companies working on their own.

It might be instructive to turn to a review of the circumstances in which people come to radiologists for diagnostic or therapeutic procedures. Essentially there are two routes. The majority of persons are referred to radiologists by other physicians who are responsible for their health care. The second route is via the patient's voluntary participation in some type of screening program which involves an x-ray examination not dependent upon any particular symptomology or a physician's decision.

In the clinical situation, a radiology referral stems from a decision by a physician that the diagnostic process requires information which can only or optimally be obtained by one or more radiologic imaging procedures. The referral may be written or verbal. Ideally it will specify not only the requested examination but also the suspected problem. For routine examinations, the consultation normally is made without challenge by the radiologist. Unless the radiologist feels he should repeat the history and physical examination upon which the clinician based his referral decision, the radiologist usually accepts the clinician's judgement about the need for the x-ray study.

For more complex and potentially hazardous procedures, radiologists routinely consult with clinicians prior to making such examinations. Such consultations are common when requests are made for several procedures or when requests are made to examine small children, women who are possibly pregnant or others requiring unusual care.

The radiologist's finding is then communicated to the referring physician where it is added to other information to form a clinical diagnosis. In some instances, the radiology finding provides the definitive diagnosis. The sore ankle is seen to be fractured. Or, no fracture is seen. Either finding is equally valid, since it determines the proper course of treatment.

Most diagnoses are more complex. The radiology finding may be only part of the information needed for a definitive diagnosis. For instance, a suspicious x-ray shadow in the lung might lead to a biopsy to determine whether it is benign or malignant. A failure to demonstrate a stomach ulcer may rule out that cause without identifying other causes of a stomach ache.

All of this has led in recent years to a concept called radiologic efficacy. This refers to the potential for the chosen examination to contribute to the diagnosis, management and eventual outcome of the patient and his problem. If it is presumed that a well-conducted x-ray examination will produce the information it is designed to produce, the questions become (1) was the proper examination requested, and (2) was the patient properly chosen to be examined.

Such determinations are medical decisions, made individually by each physician for his patient. As such, they do not constitute a proper sphere for regulation in our opinion. However, there are valid generalizations which can be drawn.

The enclosed paper by Loop and Bell (enclosure 5) was one of the earliest reports on the concept of radiologic efficacy. Their preliminary study is now being continued by colleagues in Seattle with early indications that skull x-ray examinations on emergency room patients can be curtailed by the application of efficacy criteria.

For the past five years, a committee of the American College of Radiology has been engaged in designing, testing, and applying in a limited area the concept of radiologic efficacy as an influence upon the clinician. A report (enclosure 6) prepared in the summer of 1977 summarizes the status of the effort when its principal funding expired. The College regards these conclusions as preliminary but promising. The ACR efficacy study does represent the largest and only national effort of the sort ever undertaken. Since it began, others have undertaken more limited studies. All are needed.

In addition to the clinical setting in which a physician makes a specific determination of his need for results of an x-ray study, there are two other medical situations in which x-ray examinations are performed. These involve annual or other routine physical examinations of which one or several x-ray examinations may be parts, and the chest x-ray examination required upon admission to many hospitals.

Questions have been raised about the value of routine physical examinations, with or without x-ray studies. Without attempting to discuss the whole philosophy of preventive medicine, the ACR has suggested that if a comprehensive examination is warranted, for whatever the reasons, then appropriate x-ray studies should be included.

In recent years, radiologists have developed a position about hospital admission chest x-ray examinations. Such examinations have two purposes.

One is to identify health problems which might affect the patient's care while he is in the hospital. For example, a surgical patient requiring anesthesia should be studied by x-ray to assure that he does not have respiratory or anatomic problems which would complicate the anesthetic administration. However, if the patient has received an x-ray examination just prior to admission as part of the diagnosis leading to hospitalization, its repetition is seldom warranted. All of this might say that, for the patient's benefit, special circumstances and the absence of recent x-ray examinations may be reasons for an admission chest film. The second purpose of the admission chest study is to protect other patients from contagious disease. When tuberculosis was a more common problem, many tuberculosis patients were discovered with admission chest x-rays and were isolated from other patients in the hospital. This was a particularly acute problem in obstetrical services. Where pockets of tuberculosis remain, hospitals serving those populations are justified in requiring admission films.

Beyond these circumstances is an area of medical x-ray application termed screening. In such programs, groups of people with no symptoms are encouraged to undergo x-ray examinations without prior consultation with physicians.

The most famous of these programs was the national effort to eradicate tuberculosis. Local groups sponsored mobile x-ray units which made examinations available at schools, shopping centers and other convenient sites. In 1972, the ACR joined with the American College of Chest Physicians and the PHS Bureau of Radiological Health in recommending that community based screening programs be discontinued. The reason was that relatively few new cases of tuberculosis were being detected by that method. The recommendation noted that special populations might warrant continued screening. It also noted that tuberculin skin tests could be substituted for chest x-rays, particularly for children. Even so, some states and cities still require annual chest x-rays for certain occupational groups such as teachers and food handlers.

More recently, new federal occupational health programs have mandated chest x-rays and other examinations for several categories of workers as a means of determining retirement and workmen's compensation benefit eligibility. Coal miners, asbestos workers, coke oven workers, workers exposed to inorganic arsenic are all mandated for periodic chest x-ray procedures under existing laws and guidelines. Perhaps a third of a million coal miners are entitled to such examinations. The Department of Health, Education and Welfare estimated that as many as 11 million workers with asbestos might have some asbestosis. Other workers in dusty environments are the subject of current studies and proposals. The National Institute for Occupational Safety and Health is just beginning the third round of its chest x-ray examination program for active coal miners. The ACR Task Force on Pneumoconiosis has advised NIOSH on its programs since they began in 1970.

One other population group which has attracted recent attention regarding possible benefits from x-ray screening are women over the age of 35 for breast cancers. Radiologists have developed a special x-ray technique called mammography, principally over the past 20 years. During that time, the clinical reliability of mammography, the precision of its techniques and the levels of radiation exposure have all been improved significantly.

As the National Cancer Institute's consensus panel stated last September, there is no contention about the value of mammography for any woman whose physician discovers suspicious findings in her breast. The use of mammography to survey women over the age of 50 and to survey women with personal or family history of breast disease at any age is also universally supported.

However, there have been questions raised about the propriety of screening women between the ages of 35 and 50 who have no personal or familial high risk indications. Two issues were raised by critics of mammography. One related to whether the yield of disease would be sufficient to justify the time and expense to all concerned. The second related to concerns that the radiation exposure of millions of women would at least theoretically contribute to the induction of additional breast cancers.

In June of 1976, the ACR adopted a recommendation that a "baseline mammogram" be made on women between their 35th and 40th years to look for patterns thought to be indicative of breast cancer susceptibility. The NCI consensus panel did not concur.

The evidence on both sides of the argument is mostly statistical. From the 280,000 women who have participated in the breast cancer detection center program sponsored by the NCI and the American Cancer Society, some 2500 breast cancers were detected in the first two annual examinations. The screening consisted of physical examinations plus mammograms, with the mammograms contributing to the detection of nearly 90 percent of the cancers found. In 47 percent, only the mammogram was indicative of the presence of the small cancer later confirmed by pathologic examination.

The question of whether 2500 cancers in 280,000 women is a significant yield is a social rather than a scientific one. However, those were actual cancers discovered, and not statistical estimates from extrapolations. The argument that mammography might be causing cancers is based entirely upon extrapolations and not upon any observed instances of cancer induction.

In 1970, a federal interagency working group attempted to project radiation uses and exposures to the end of the century. Their conclusion concerning medical radiation was that the utilization of ionizing radiation would continue to rise but that improvements in technology would tend to offset increased numbers of exposures by allowing diagnostic results from smaller amounts of radiation. This conclusion appears to remain valid.

IV Current professional intitiatives in radiology

It was only weeks after the discovery of x-rays that scientists and physicians recognized both their usefulness in medicine and their potential hazards. Indeed, the first efforts to use x-rays to treat cancers and skin diseases began weeks after the news of the discovery reached North America. From that time to this, radiologists have felt a responsibility to their patients, their co-workers and to themselves to study radiation phenomena, to develop more efficient examination and treatment procedures and to reduce the radiation levels necessary to achieve their diagnostic and therapeutic objectives.

As noted, radiologists prompted the first federal initiative on radiation at the National Bureau of Standards in 1928. Radiologists were involved in the development of the atomic bomb during World War II. Their urging later resulted in the highly productive programs of the Atomic Energy Commission's Division of biology and medicine. The ACR strongly supported the establishment of what is now the Bureau of Radiological Health in 1957. Two years, later the College testified in support of the Atomic Energy Amendments of 1959, which led to state radiation control programs. The College assisted in the drafting of model state laws for equipment registration and regulation.

During the 1950's, the ACR campaigned against the use of dangerous fluoroscopic shoe fitting devises. The College collaborated with the American Academy of Pediatrics to urge pediatricians to abandon routine use of fluoroscopes on children.

In the early 1960's, the College developed a strong program to prepare radiologists to deal with the effects of radioactive fallout, then threatened from nuclear weapons air tests in this and other countries. The College took the position that the radiologist was the one person in most communities who knew enought about ionizing radiation to understand potential problems and to furnish guidance to civil defense authorities. The program won several citations for its effectiveness.

In the late 1950's, the College produced a comprehensive set of teaching materials on radiation safety practices. In 1970, it collaborated with the Bureau of Radiological Health in the preparation and distribution of more than a half million copies of a monograph, "X-ray Examinations: a Guide to Good Practice" which updated some of the information in the earlier materials. The College soon will publish another guide to radiation safety uses, this one directed to radiologists and providing much greater detail.

In 1970, the College began a series of projects designed to help the National Institute for Occupational Safety and Health to implement its responsibilities under the 1969 Coal Mine Health and Safety Act. Out of that cooperation came a series of teaching programs which have been expanded to a variety of radiology subjects.

Also out of the coal mine chest experience has come a current common dedication to quality assurance which is shared by the College, the x-ray industry and BRH and NIOSH for the government.

During the 1960's, the College began a practice assessment program by which radiologists could obtain peer review of the manner in which they performed their professional duties. In 1965, the College under contract with the National Cancer Institute began a series of projects to develop techniques of mammography and to make them available to radiologists and patients across the country. In this decade, the College collaborated with BRH in the development of the distinctive radiology learning laboratory which has become a standard teaching module in almost every American medical school. The laboratory consists of come 4000 x-ray films with proven diagnoses plus physics and biology materials.

Other innovative teaching programs included home study and self-evaluation kits, weekend seminars for radiologists and other physicians, television tapes, syllabi in physics and radiobiology, course materials for radiologic technologists. The 1200 formal schools of x-ray technology are the largest group of allied health professional educational programs in the health field. Radiologists serve as medical directors of these schools. The College is a co-sponsor of the 55-year old American Registry of Radiologic Technologists, the nationally recognized voluntary accrediting agency.

Within this decade, the College cooperated with BRH in the development of a program to encourage the use of gonad shields for x-ray examinations of the abdomen. An effective gonad shield for males was developed and distributed by the College to all its members. Female gonad shields have been less effective because the ovaries more often lie within the abdominal area of interest and cannot be protected without losing the diagnostic information sought from the procedure.

In 1972, the College worked with the American Academy of Orthopedic Surgeons, the American Occupational Medical Association and NIOSH to conduct a seminar on the use of low back x-rays in pre-employment examinations of workers in strenuous occupations. The same year, the College began the design of the efficacy study described above with support from the Public Health Service.

For the past two years, the ACR has co-sponsored one or more days of the annual program of the Conference of State Radiation Program Directors, to discuss medical radiation problems and initiatives.

V Federal radiation programs

The article by Moseley and Linton (enclosure 1) was intended to indicate the range and redundancy of federal activities directed toward medical uses of ionizing radiation. It led one observer to recall the comment that "Many are grateful that we get less government than we pay for."

The single scientist at the National Bureau of Standards in 1928 led to a radiation physics section there which still functions on vital measurement activities. He also led to the organization and shepherding of the National Council for Radiation Protection and Measurement which was supported by NBS until it received a federal charter in 1963.

The Atomic Energy Commission's activities after World War II encompassed both regulation and development in a balance which produced tremendous breakthroughs in diagnosis and therapy. Subsequent to the division of the AEC into the Nuclear Regulatory Commission and the Energy Research and Development Administration, much of the impetus for medical isotope development has been lost. Now the Department of Energy funds only a small program.

Formal Public Health Service radiation protection interests were funneled into the Bureau of Radiological Health. Its primary mission subsequent to the passage of PL-90-602 and its assignment to the Food and Drug Administration has emphasized regulation. However, its educational programs remain significantly broader and more productive than any other similar activities within the FDA.

One result of the 1959 Atomic Energy Amendments was the creation of the Federal Radiation Council, a cabinet-level policy coordinating body. The FRC produced a series of federal policy statements during the 1960's on occupational and environmental radiation levels which are still in effect. The FRC was folded into the Environmental Protection Agency in 1970. The EPA Office of Radiation Programs has been active since then.

In 1972, the Food and Drug Administration ended an inter-agency agreement with the AEC under which it had abstained from controling radioactive drugs. Since that time, FDA's Bureau of Drugs has implemented a program to control the manufacture of radiopharmaceuticals comparable to its programs for other classes of drugs. It is a compliment to the Bureau of Drugs that it implemented its program without disrupting the supply of radiopharmaceuticals to physicians and patients.

In may of 1976, the FDA took on greater responsibilities for medical devices under PL 94-245, as sponsored by this committee. The FDA's Bureau of Medical Devises and Diagnostic Products created a radiology panel and classified some 250 products used in radiology under the scheme specified in the law. Redundancies between on-going BRH programs and those initiated by BMDDP have not yet been eliminated by FDA.

Support for research into diagnostic and therapeutic radiology has been lodged within the several National Institutes of Health. In particular, programs of the National Cancer Institute have been supportive of radiation therapy initiatives for cancer treatment. Therapeutic radiologists have served as advisors to the NCI and sit on many of its regular and adhoc study groups. Support for research in diagnostic radiology has fared less well. The National Institute of General Medical Sciences has been designated as a program center. However, current initiatives receiving support from NIGMS are meager. In the fall of 1977, the director of NIH responded to requests from academic radiologists to study the support at NIH for diagnostic radiology. An ad hoc committee is expected to report soon on its conclusions and recommendations.

VI Radiation risks and their estimates

At the 1928 International Congress of Radiology in London, American radiologists participated in the organization of the International Commission on Radiological Protection and the International Commission on Radiation Units and Measurements. Parallel national efforts were created within the National Bureau of Standards, the NCRP. After World War II, the US began participation in the United Nations Scientific Committee on the Effects of Atomic Radiation and the International Atomic Energy Agency.

The Federal Radiation Council issued a series of policy papers in the 1960's, In 1956, a committee of the National Academy of Sciences had issued a report on the biologic effects of atomic radiation (BEAR). In the final months of the FRC's function, it responded to congressional and other requests by contracting with the NAS for a second study in the same area. That report, "Biologic Effects of Ionizing Radiation" (BEIR) was completed in 1972. A subsequent committee of the NAS is now completing a revision of the 1972 report, having contributed a report on cost-benefit calculations for radiology in the intervening years.

The several reports dealing with radiation risks and assessments from the NAS, the NCRP, UNSCEAR, the ICRP and others are discussed in the introduction to the as yet unpublished ACR new guide for radiologists. The introductory pages are inserted below and the entire text is attached (enclosure 8).

1. INTRODUCTION

This report supersedes and replaces X-Ray Examinations......A Guide to Good Practice, which was published in 1971 by the American College of Radiology, in cooperation with the American Medical Association and the United States Public Health Service. That Guide was intended for all physicians involved in decisions to perform x-ray examinations. It emphasized the considerations necessary for such decisions and reviewed principles of good practice in the use of x-ray equipment. It stressed the undisputed benefits of medical diagnostic radiology, on which one-third to one-half of all important medical decisions probably depend. The Guide stated that, in almost every medical situation, potential radiation hazard should not be a contraindication to a radiological examination from which a physician might reasonably expect to obtain information influencing the medical care of a patient.

Since the Guide was written, several scientific reports have been published giving estimates of risk from exposure to ionizing radiation. Some of these reports differ from others substantially in their conclusions and recommendations, although all are based on essentially the same data. None of them negates the basic premise of the Guide, but they do call for further amplification and discussion for the information of the radiologist.

Among these publications are: a report on basic radiation protection criteria from the National Council on Radiation Protection and Measurements (NCRP); a two-volume report from the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) on levels and effects of ionizing radiation: and a report from the Advisory Committee on the Biological Effects of Ionizing Radiations (BEIR), National Academy of Sciences-National Research Council, on the effects on populations of exposure to low levels of ionizing radiation. (The UNSCEAR and BEIR reports were based on essentially the same information but are markedly different in analysis, presentation and conclusions.) In addition, the second national x-ray exposure study (XES), organized by the PHS Bureau of Radiological Health, provided new data on actual exposure levels from diagnostic radiology in the United States in the year 1970. This permitted new calculations of genetically significant dose (GSD) to the United States population from medical radiology; during the analysis of the data, errors in the 1964 (XES) data published earlier were identified and corrected. Also, a monograph by Brent and Gorson provided a literature summary and commentary on the problems of radiation exposure in pregnancy.

Radiologists are concerned in their daily work with radiation effects and radiation protection. Many recommendations are offered to them, and at times these recommendations are found to be mutually incompatible. A major source of the confusion is that some advice is based on the 1972 UNSCEAR report and on prior and subsequent NCRP reports, while other advice is derived from the 1972 BEIR report. The latter differs from the others in significant ways. It sets numerical estimates of risk at low radiation levels, in terms of numbers of additional deaths from cancer per year, by extrapolating from epidemiological data obtained at much higher radiation levels. The body of the BEIR report stressed the variables that might make such linear extrapolation invalid as a means of estimating risks at low doses and dose rates, but the recommendations appeared in the summary of the report without reflecting these reservations.

A reader could easily conclude that the estimates in the summary were established facts with sound scientific basis.

The UNSCEAR report, on the other hand, stated that data obtained at high doses and various dose-rates should not be used to estimate even upper limits of risk of radiation-induced cancer at low doses and other dose-rates, in view of the variables involved and the danger of gross over-estimates. A report published by the NCRP in 1975 provides a comparison and analysis of the data bases, approaches and conclusions of the BEIR, UNSCEAR and other recent assessments which is helpful in understanding the differences among them. Nevertheless, the divergence between the UNSCEAR and BEIR opinions remains a source of confusion to radiologists, in terms of the difference in interpretation of epidemiological evidence as utilized in the two reports.

Properly chosen and carefully performed x-ray examinations are an indispensable part of modern medicine. However, radiologists and their medical colleagues must always consider the problem of determining a specific course of action for a specific patient, in the context of current knowledge of the benefits and the potential risks of radiation. Some medical care of a patient is always the primary consideration in assessing needs for diagnostic radiological procedures. Good radiological practice may dictate modifications of diagnostic procedure in certain circumstances; such decisions must be made by responsible physicians in individual cases. Radiation exposure which does not contribute to the purpose of the examination, and which can be avoided by reasonable measures, is not good practice.

From these comments and those of many others, it can be seen that physicians and other scientists can view the same evidence and apply the same analytical methodologies to arrive at significantly different conclusions. Indeed, several earlier witnesses before the subcommittee have presented viewpoints radically different from the consensus opinions of their peers as reflected in reports of the NCRP, ICRP, UNSCEAR and NAS committees.

Like many other biological reactions, radiation effects are most easily studied in the instance of gross insults to living organisms. The only group of humans subjected to such insults in large populations were the Japanese present at Hiroshima and Nagasaki on August days in 1945. These populations have been studied extensively by joint Japanese-American teams ever since and their experience has contributed to our radiobiological knowledge.

Most researchers have worked with mice and other experimental animals. Their results have required extrapolation to humans after suitable accomodation to interspecies differences.

Much of the research with human populations has been epidemiological, relying upon questionnaires, records searches and estimates of doses based upon inadequate information for the sake of comparing irradiated groups with control populations.

There are known and observed biological effects of the irradiation of humans and other species at levels of 100 rads and above. Some effects have been observed at levels of 25 rads and a very few papers have suggested cell-level effects at less than 20 rads. One Israeli paper reported effects at doses estimated to be 6.5 rads, Thus, conclusions about individual or population effects of exposures in the one to two rad range employed in diagnostic radiology are generally based upon the extrapolation of observed effects downward from higher levels. This involves the use of what is called the linear, non-threshold hypothesis. This presumes that the amount of change caused in a living creature by radiation doses is directly proportional to the amount of radiation received. If a dose of 100 rads produces an effect scaled at 100 units, then one rad will produce one unit of effect though unmeasurable in individuals, and a tenth of a rad would produce a tenth of a unit of effect and so on and downward to zero. The application of the linear, non-threshold concept must remain hypothetical, capable neither of proof or disproof as it concerns low levels of radiation.

The linear, non-threshold hypothesis has been described in NCRP publications as a "worst case hypothesis" since some of its assumptions are known to be excessive. These include assumptions that partial body exposures and the cumulative effect of repeated small doses are identical to the same total dose in a single exposure. It also presumed that there is no effective biologic repair of radiation injuries. If the second presumption were correct, then high energy radiation could not be used to destroy cancers while preserving the general health of the patient.

Some authors recently have suggested that low level radiation effects can be presumed which are worse than linear. The Environmental Protection Agenc- announced that it would use the linear, non-threshold hypothesis as the basis of its policy establishment for federal radiation facilities.

Several statistical conventions have been employed by radiobiologists and epidemiologists to express the magnitudes of risk presumed to accompany low diagnostic and other radiation exposures. For example, to describe the risk of inducing breast cancer in women by subjecting them to mammography, Dr. Arthur C. Upton began with the natural incidence, expressed as seven per thousand over a lifetime. (.007). If a mammographic examination involved one rad of dose to the midplane of the breast, he estimated that it would increase the risk by 1 percent to (.00707).

This is related to another radiobiological concept known as a doubling dose, which refers to the amount of radiation assumed to double the probability of effects upon the tissue radiated. Thus, using Upton's numbers, 100 mammograms at one rad each would be needed to double the risk to 14 per thousand or 0.014. Since doses to the breast with recent developments in mammographic technique are now a fraction of a rad, the calculations would overstate current risks, though they were appropriate prior to the introduction of low-dose films in 1976.

These mixtures of biology, statistics and social policy are common grist for learned journals and societies. They impose a burden upon congressmen and public leaders who find themselves obligated to arbitrate contrary conclusions drawn from the same data base, often utilizing similar methodology.

VII Current radiological concerns with federal programs

When the College testifies before congressional committees, we attempt to be constructive. We support more legislation than we oppose. If we object to a specific proposal, we attempt to explain why and to offer an alternative approach. At times, we have stated that some proposals represent an unjustified and unproductive federal invasion of medical practice and medical judgement.

The three concerns expressed in our introduction relate to the administration of federal programs, rather than to any legislative flaws. However, oversight hearings are a forum for the expressions of concern about administrative shortcomings, whether these are best remedied by better management or by new legislation.

Our first concern is for the continuing lack of a focus for medical radiation uses and control programs within the Department of Health, Education and Welfare. By extension, there is even less focus for federal efforts on health uses of radiation among the other federal agencies which have some responsibility for ionizing radiation

We think it vital that any necessary federal regulation of health uses of ionizing radiation and health effects of ionizing radiation be lodged in an agency which has primary health and biological science responsibilities. The objectives of health uses of radiation are the diagnosis or treatment of disease. The decisions to use radiation are medical decisions. The science which supports these uses is physical and biological science. The objective of any federal regulation of radiation uses is to protect the health of those involved in the several context of radiation applications.

Thus, we favor the Department of Health, Education and Welfare as the federal lead agency on radiation programs. However, we also favor great improvements in the performance of Public Health Service agencies in this respect. And we strongly favor the elimination of duplicatory and competitive jurisdictions over radiation science within DHEW and between DHEW and other federal agencies. In this latter respect, we favor the restoration of a Federal Radiation Council, along the lines of the agency of that name which functioned for a decade until 1970.

Our preference for the Department of Health, Education and Welfare as the lead federal agency on ionizing radiation uses is based upon the philosophy expressed above rather than our unstinting admiration for its fulfillment of radiation responsibility.

We do think that implementation of the mandate in PL 90-602 for performance standards for diagnostic x-ray systems has been accomplished carefully and professionally. The Bureau of Radiological Health is to be commended for avoiding haste and rigidity which would have inflated costs without adding to the safety of equipment. BRH is also to be complimented for its efforts to train radiation safety manpower for state and local programs. We salute further its considerable efforts to support the education of physicians, technologists and other professionals who use radiation in medicine.

Speaking to our second concern, we have criticized the Food and Drug Administration for its duplication of responsibility for radiological products since the enactment of the medical device law in 1976. Despite the competence of BRH in this area, the Bureau of Medical Devices and Diagnostic Products was allowed to establish a separate bureaucracy and advisory group to deal with radiology products. The advisory group has been frustrated by the insistence of the FDA upon fitting well-defined radiology devices only used by physicians and technologists into patterns designed for appliances to be used by patients without supervision. We are told that these conflicts are being resolved so that radiologists and manufacturers may be able to relate to a single responsible and competent agency. We hope so.

In the past two or three years, we have been beset by what can only be called "turf wars" among the several federal agencies asserting authority over radiation uses.

The BRH issues "guidelines" which are not regulations and are not mandatory but which represent an assertion of federal domain. The FDA Bureau of Medical Devices and Diagnostic Products has issued its "good manufacturing practices" protocol which potentially could be extended to any product used in health care, including ballpoint pens and janitor supplies. The Environmental Protection Agency has issued guidelines for federal health facilities to control their use of medical radiation. Separately, it issued a policy statement asserting that it will use the linear, non-threshold hypothesis as its basis for making decisons.

Recently, the Nuclear Regulatory Commission issued new proposed regulations for medical users of radioactive materials. Its prefactory statement asserts an intent to withdraw from regulation of medical users of radionuclides. However, the substance of the proposal contradicts that intent. In several spots, the NRC notes that its proposal is inconsistent with current regulations of the Food and Drug Administration's Bureau of Drugs. The Burea of Drugs assumed responsibility for the manufacture of radiopharmaceuticals in 1971.

All of medicine is indebted to the Atomic Energy Commission for its careful fathering of the uses of radionuclides in medicine, its support of training programs for physicians and technologists and its enlightened licensing procedures. However, we have 25 states which control the same radioisotopes plus well defined and well established professional standards for training and qualification. A new surge of regulation by NRC is redundant.

All of this leads us to reassert a strongly felt need for somebody to get things organized on behalf of the federal government. When the White House recently decided to respond to initiatives of this subcommittee and look at problems resulting from low level military and occupational exposures, it designated the Department of Health, Education and Welfare as its lead agency. Since these were health-related problems, we think the initial referral was appropriate.

Neither the Environmental Protection Agency nor the Nuclear Regulatory Commission were involved at first. DHEW Secretary Califano gave the problem to his Office of General Counsel, rather than to the Public Health Service and to the Food and Drug Administration, where the department's competence is found. Some good people from various agencies are involved though most of them are essentially out of their area of competence.

During the decade when the Federal Radiation Council existed, it provided a cabinet-level mechanism for defining policy and responding to problems affecting more than one federal agency.

We now urge the creation of a new Federal Radiation Council, again as a high-level coordinating agency. It should not have direct program responsibility which would put it into competition with line agencies. It should have a small staff with scientific competence and a budget sufficient to allow it to support studies by the National Council for Radiation Protection and Measurements and other responsible scientific groups. Had such an FRC structure existed now, the President would not need to create an ad hoc arrangement. Indeed, the several agencies might have made a more coherent presentation to this subcommittee last spring if their efforts had been coordinated.

Turning to our third concern about the impact of cost containment efforts on the development of new radiological technology, we note the example of the computerized tomographic scanner. This marvelous new machine has been the trial horse for the health planners. Ironically, the strictures of the planning mechanism have hastened the medical acceptance of CT scanners as hospitals scrambled to be the only institution in town allowed to have a scanner. The more orderly process of technical development and clinical trial has been telescoped to meet demands of planners for detailed answers of cost-effectiveness and medical efficacy.

• Enclosures 5, 6, 8, and article "Radiology Manpower Update, 1976 Shortage or Surefit?" mentioned in Dr. Morgan's prepared statement may be found in the subcommittee files.

The CT scanner is an expensive piece of equipment. Its use is a substantial expense to a community. But its value is also significant, both in quantifiable savings of patient bed days, patient trauma, elimination of other procedures and in the unquantifiable aspect of better health care. We remain hopeful that the necessary concerns for cost reductions will not entirely obliterate any other concerns for health care.

Yet, we have cause to be doubtful. After more than 19 months, we are still waiting for instructions from the Health Care Financing Administration to Medicare carriers to reimburse physicians and hospitals for body CT scans. There is no real issue remaining to be resolved. However, it still appears that at least several more months of bureaucratic obfuscation may elapse before carriers can begin reasonable reimbursement. In the meantime, Medicare beneficiaries are given less effective diagnostic procedures which are covered, the patient is required to pay or else the doctor and the hospital swallow the costs.

CT scanners are not our only concern. Radiation therapy generators, the special complex x-ray equipment needed to study motion in the heart or brain and even general purpose radiographic-fluorographic equipment all range in price above levels set by planning laws and regulations. If too stringent restrictions dry up the market, industry will not be able to support research and the development of better, safer, more efficient radiology systems will effectively cease. If current private industry efforts must eventually be supplanted by federally subsidized development, we shall all be the losers.

In brief, these are our current concerns and suggestions. We respectfully request the acceptance of our entire testimony and enclosures for the hearing record. We will be happy to respond to any questions.

The Federal Government's Impact on Radiology

ROBERT D MOSELEY, JR [1] AND OTHA W LINTON[2]

The areas of involvement by federal agencies which have primary health missions are outlined The roles of many federal agencies which touch on health peripherally are also discussed

Legislative and regulatory activities of the federal government have achieved a dominant influence over the future of radiology This primacy is achieved by the assertion of an all pervading federal authority or responsibility for nearly all aspects of radiologic practice technologic improvements, licensure and certification facilities, materials (drugs and devices) research, personnel management standards and measures, manpower recruitment, compensation, and professional relationships

Federal performance standards for existing radiologic equipment have been promulgated during the past few years The introduction and proliferation of new devices (e g , computed tomography) have come under federal controls for radiation safety, regional health planning, and cost containment The distribution of physicians geographically and by specialty is already influenced by federal support for residency programs and has come under stringent review by planning groups

The multiple roles of the federal government in health care specifically in radiology, pervade all three constitutional branches They are found, as well, in those quasiadministrative quasijudicial agencies (e g , Federal Trade Commission) which regulate much of the nation's commerce

A half-dozen congressional committees have direct legislative responsibilities in medical economics, health manpower, and radiation safety Other committees have jurisdiction over matters that have periodic impact on radiologic practice, such as the transportation of radionuclides on scheduled airline flights or standards for chest x ray examinations of coal miners

The executive branch is omnipresent in health care The largest group of regulatory and funding programs is lodged within the Department of Health, Education, and Welfare Medicare, Medicaid, health manpower, planning research, and drug and device regulation are all major HEW programs Equally vital are programs such as occupational medicine, workmen's compensation and fair labor practices within the Department of Labor, policies of the Immigration and Naturalization Service for foreign-trained physicians, radiation standard setting functions of the Department of Commerce through the National Bureau of Standards, and federal subsidies for new technology development from the National Science Foundation

The federal judiciary is not normally the court of first resort for litigation involving radiologists Issues such as the tax status of professional corporations and allegations of antitrust violations by medical societies do originate in federal courts The elasticity of the interstate commerce clause of the Constitution also means that appeals from malpractice actions and enforcement of product safety guarantees in federal legislation may reach federal district or appellate courts

Under the federal system, much legislation dealing with health requires a partnership in regulation and funding with state and local governments The health planning programs established by Public Law 93-641 in 1974 are an example State and local governments and newly created regional agencies are given roles in planning for health facilities The involved federal health agencies attempt to establish broad guidelines Actual determinations of policy and choices among contenders for expansion of facilities are made at the local or state level It is common in federal health legislation to give the states 24 months to enact conforming laws and to provide federal subsidies for state agencies with enforcement responsibilities A more permissive form of such cooperation resulted from the 1959 Atomic Energy Act This established the "agreement state" provisions, by which states could assume control of radioactive materials from the Atomic Energy Commission by passing laws acceptable to the AEC Currently 25 states have chosen to take such responsibility, leaving the Nuclear Regulatory Commission to continue supervision in the rest of the country

The payment mechanism brings federal pressures on providers of health services, as well as upon state and local governments Physicians do not have to scale their charges to the 75th percentile of local usual, customary, and regular fees, but that amount is all they will be paid for services to beneficiaries of federal programs Many health insurance programs are carriers or intermediaries for Medicare Federal decisions often are adopted by the private plans, both in terms of fee levels recognized and in terms of services covered For example, last summer just before the Social Security Administration corrected an inadvertent limitation on coverage of head CT scans, several insurance carriers announced their intent to impose a similar limitation

The federal health purse is too large to be ignored by physicians as individuals or as a group In 1976, the nation

---

Received February 28 1977 accepted March 7 1977

[1] Department of Radiology University of New Mexico School of Medicine Albuquerque New Mexico 87131 Address reprint requests to R D Moseley Jr

[2] Governmental Relations American College of Radiology Chevy Chase Maryland 20015

spent $139 3 billion on all health services and costs, including support for education, research, construction, and the care of millions entitled to health benefits under existing programs according to Social Security Administration estimates This represents a 14% increase over the revised estimate of $122 2 billion for 1975 The 1976 estimate works out to a per capita expenditure for health care of $683 The figure for this year includes about $59 billion in public spending $40 billion in federal funds, and $19 billion from state and local sources

Besides payments most federal health programs and regulatory efforts now contain provisions for penalties against physicians who violate their provisions The legislative demand for strict enforcement and greater penalties is likely to produce action in the Ninety fifth Congress which began January 1977

Areas of federal responsibility toward medical care and particularly toward radiology can be categorized under eight broad headings

1 Reimbursement of physicians and hospitals for services to beneficiaries of various publicly supported health care programs, such as Medicare, Medicaid, Veterans Administration, and Department of Defense health activities

2 Influence on patterns of practice through health planning activities and stimulation of health maintenance organizations

3 Influence on the geographic and specialty distributions of physicians through training subsidies to medical school and residency sponsors and through the National Health Service Corps

4 A concern for the quality and appropriateness of medical and hospital services delivered to beneficiaries of federal health care programs as manifest in the creation of professional standards review activities, utilization review requirements, and the encouragement of private health care insurers to undertake similar activities

5 Regulation of drugs, medical devices, and diagnostic products by the Food and Drug Administration to insure safety and efficacy

6 Support for research in basic and clinical areas and into the socioeconomic milieu of medicine

7 Support for construction of medical facilities and provision of equipment under successor programs to the Hill Burton Act within health planning concepts

8 Regulations and efforts to assure safety of ionizing radiation uses in medicine These include establishment of standards, licensure of radiation sources, personnel requirements, monitoring of exposures, and radiobiologic investigations

In all of these areas, the responsibilities and funding of several federal agencies substantially overlap For example, a recent unpublished study by the American College of Radiology turned up more than 3,000 research projects on ionizing radiation supported by various federal agencies Much of the support came from the Department of Health, Education, and Welfare through the National Institutes of Health, and from the Food and Drug Administration through the Bureau of Radiological Health However, other radiation research is sponsored by the Department of Defense, Veterans Administration, National Science Foundation, Energy Research and Development Administration, Environmental Protection Agency, Department of Commerce through the National Bureau of Standards

On the regulation of radiation sources and uses, there is overlapping jurisdiction among the Nuclear Regulatory Commission, Bureau of Radiological Health, and Environmental Protection Agency The Environmental Protection Agency claims a broad mandate to advise the president on all matters of federal radiation policy on the basis of its succession to the role of the now defunct Federal Radiation Council The Bureau of Radiological Health claims jurisdiction over electronic products including x ray machines under the 1968 Electronic Products Safety Act, and also a general authority over medical radiation uses under sections of the Public Health Service Act In addition, the FDA's Bureau of Drugs and the new Bureau of Medical Devices and Diagnostic Products also assert responsibilities for manufacture of radiopharmaceuticals and generally for safety and efficacy of all medical devices Though the Nuclear Regulatory Commission yielded control of the isotopes, it has retained control over licensees in the nonagreement states

To complicate the radionuclide picture further, the shipment of radioactive materials is the responsibility of the Department of Transportation, where various agencies address problems of air, surface, and water carriers

To present an overview of the pattern of federal interests in radiology, an outline of organizational responsibilities has been prepared It is meant to be indicative, rather than inclusive The interests suggested for each agency are not the only ways in which it may relate to radiology or medicine

Congress

1 Joint Committee on Atomic Energy authorizes programs of the Nuclear Regulatory Commission and the Energy Research and Development Administration including regulations for uses of isotopes and funding for further development of nuclides (eliminated in Ninety fifth Congress)
2 Senate Commerce Committee has jurisdiction over electronic products act and its successors, and over transportation of radioactive materials
3. Senate Finance Committee has jurisdiction over federal health programs involving special taxation, such as Medicare and Medicaid
4 Senate Human Resources Committee has jurisdiction through its Subcommittee on Health for those federal health initiatives not based upon special taxation, such as health manpower, medical education, research, and construction
5 House Ways and Means Committee is the point of origin, constitutionally, of all measures dealing with taxes thus including Medicare and Medicaid through its Subcommittee on Health
6 House Commerce Committee has broad health jurisdiction through its Subcommittee on Health comparable to the Senate Labor and Public Welfare
7 House Education and Labor Committee has jurisdiction over working conditions and some educational activities

8 Senate and House Committees on Veterans Affairs and on Armed Services have jurisdiction over health care activities for active military personnel, their dependents and veterans as well as substantial funding for facility construction support for medical education and research in government health institutions

9 General Accounting Office is the investigative arm of the Congress making frequent inquiries into health programs administered by executive branch agencies GAO reports often serve as a basis for oversight hearings or new legislation

10 Office of Technology Assessment is a research organization which supports the Congress with detailed reports on various national problems such as the clinical and economic impact of CT scanners on health care

11 Other congressional committees have tangential interests when radiology involves public transportation, product safety, federal budgeting or other areas seemingly remote from health care

Executive Branch

Department of Health, Education, and Welfare

1 Food and Drug Administration

a Bureau of Radiological Health enforces electronic products act regulating such things as performance of x ray systems also has mission under the Public Health Act for education of physicians and other users of ionizing radiation

b Bureau of Drugs has jurisdiction over contrast media and radiopharmaceuticals

c Bureau of Medical Devices and Diagnostic Products enforces a new law extending federal jurisdiction over medical devices similar to classic FDA responsibility for drugs

2 National Institutes of Health

a National Cancer Institute administers the cancer attack program funds most basic and clinical research on cancer and supports cancer centers

b National Heart and Lung Institute supports activities devoted to areas indicated by its title, including projects for imaging

c National Institute of General Medical Sciences supports research projects on diagnostic radiology within its biomedical engineering branch and with relatively low priority

d Other categorical institutes

e Division of Research Grants exercises responsibility through its Radiation Study Section and other study sections for peer review screening functions to receive and review applications for grant and contract support, and to assign to appropriate federal funding agency

3 Health Resources Administration has programs dealing with health statistics research facilities manpower, and planning

4 Health Services Administration has programs dealing with Public Health Service hospitals Indian health, professional standards review, health maintenance organizations, and National Health Service Corps

5 Social Security Administration

a Bureau of Health Insurance administers Medicare program

b Bureau of Disability Insurance administers federal workmen's compensation and disability programs including coal miners' black lung disease benefits program prior to 1973 and continuing

6 Social and Rehabilitation Service administers federal portion of state Medicaid programs through Medical Services Administration

7 Office of Education has responsibility for vocational education programs including funding for training of allied health personnel

8 National Institute for Occupational Safety and Health has responsibility for programs in areas indicated by title including coal miner chest x ray examination and surveillance of other mining industries

9 National Library of Medicine is the central federal repository of books magazines and audiovisual aids dealing with health, also has extensive reference service

Other Executive Branch Agencies

1 Veterans Administration manages the largest medical care system in the world providing care to veterans of military service

2 Department of Defense

a Assistant secretary for health and environment plus surgeon general of military services operate health facilities for active military and dependents

b CHAMPUS, program for civilian health providers of services to military and dependents

c Armed Forces Institute of Pathology is the noted repository of disease materials on slides and radiographs, has consultant and teaching facilities, including American Registry of Pathology, Registry of Radiologic Pathology and Registry of Radiation Pathology

d Armed Forces Radiation Research Institute conducts radiobiological studies

3 Energy Research and Development Administration supports a program of research on radionuclides for medical application

4 Nuclear Regulatory Commission continues to control medical uses of nuclear byproducts in states not having agreements for such regulation, also sets national requirements for health standards of contractors and licensees

5 Department of Transportation, through the Office of Hazardous Materials Operations and Federal Aviation Agency, supervises shipment of radioactive materials and other categories of hazardous materials by common carriers

6 Civil Aeronautics Board approves or denies tariffs governing transportation of hazardous materials, including radiopharmaceuticals, on scheduled airlines

7 Department of Labor has responsibility for working conditions in health occupations

a Occupational Safety and Health Administration has responsibility for worker safety and health programs, including coal miners' black lung disease benefits program

b Wage and Hour Division enforces minimum wage law, overtime provisions

8 Department of Commerce is involved in the importation of x ray equipment

a National Bureau of Standards performs measurements and develops basic radiation concepts through its Center for Radiation Research

b Bureau of Census works with U S Public Health Service National Center for Health Statistics in collection of data about medical care

9 Department of State conducts foreign policy, including science and medical affairs, notably designating U.S participation in the United Nations Scientific Committee on Effects of Atomic Radiation

10 Department of Justice deals with charges of antitrust violations by physicians and physician organizations under

Sherman Act
- a Immigration and Naturalization Service sets criteria for admissions of alien physicians and other health workers
- b Drug Enforcement Administration shares major responsibility for control of illicit drug traffic

11 Federal Trade Commission is an independent agency having some overlap with the Department of Justice in enforcement of fair trade act, including recent alleged violations by medical societies

12 Environmental Protection Agency inherited role of Federal Radiation Council in coordinating federal policy which is carried out through the Office of Radiation Programs. They are attempting to extend mandate beyond one of advising the president

13 National Science Foundation funds research programs and attempts to set national goals for science including medical science

14 Department of Housing and Urban Development has mortgage guarantee programs which encompass some medical facility construction

15 Civil Service Commission writes job descriptions for individuals working in federal health programs

16 National Aeronautics and Space Administration supports research on life support systems and imaging systems with medical applications

17 Equal Employment Opportunities Commission supervises federal enforcement of fair employment practices, including review of testing and certifying bodies to eliminate racial and ethnic biases

White House

1 Office of Science Advisor was recently revived

2 Office of Management and Budget coordinates and reviews programs and spending levels proposed by the excecutive branch agencies

It can be seen that, well short of the much discussed advent of comprehensive national health insurance, federal agencies already have a pervasive effect upon the practice of medicine and the specialty of radiology. In the recent presidential campaign, both the successful and unsuccessful candidates' platforms included references to efforts to decrease the federal bureaucracy. Would it be too much to hope that we could suggest a good place to start?

An editorial by Moseley and Linton appears in this issue.

Mr. ROGERS. Fine. Thank you.

Dr. Carter.

Mr. CARTER. Thank you, Mr. Chairman.

Do you think perhaps many untrained practitioners order too many X-rays; is that correct?

Dr. MORGAN. Well, I think it may have been a problem much more in the past than it is now, simply because in today's medical schools, training the physicians of tomorrow, and in the residency training programs for physicians, the impact of radiology and the importance of radiology to medical care is much more appreciated now than ever before. As a consequence, if you go into any one of our major teaching hospitals, departments of radiology are located at the crossroads of all of the activity going on in these hospitals, whether it is activity pertaining to internal medicine, surgery, so on.

Everything seems to focus in departments of radiology today, very much like it used to focus in departments of pathology when you and I were going to medical school. So I think there is the basis of good education, not only for the specialist, but for all of the medical profession, including the general practitioners who constitute the basic structure of our health care system.

Mr. CARTER. What percentage of our physicians who use X-ray machines for diagnosis and for treatment have lead-lined offices, as they should have?

Dr. MORGAN. If the State regulatory authorities, working in conjunction with the Bureau of Radiological Health, are doing what they should do, I would guess that most of them, well, all of them should have them. To what extent they actually do have them, I cannot, in my position, estimate what this might be.

But this is a kind of role that NACOR was talking about back in 1958 when it set forth that there should be a regulatory structure, not necessarily particularly complicated—at least no more complicated than need be—to deal with precisely these problems.

Mr. CARTER. Do you think it is wise for someone who does X-rays to wear a monitoring mechanism similar to that shown to us by Dr. Kennedy today?

Dr. MORGAN. Film badge or a thermolucent detector?

Mr. CARTER. Yes, sir.

Dr. MORGAN. Anybody who is employing radiation in his practice—and this includes not only physicians but also the technologists working with them—should carry such devices. Here again, there is nothing complicated about radiation control. It is largely common sense, and common sense dictates that if you are dealing with radiation, and since it is not an unhazardous modality, common sense dictates that you should know what you are getting. It is as simple as that.

Mr. CARTER. But, Doctor, common sense is the rarest of all qualities, sir, as I see it. I think that you are certainly right on that.

What do you think about the use of radioactive iodine or thorium? Do they present any danger?

Dr. MORGAN. All radiation sources, when used unwisely, present a danger. That would include any radioactive material, including the ones that you mentioned. The radioactive materials that are used for treatment, of course, usually are used by the people who do this day in and day out and are usually pretty well versed in hazards. The use of radioactive materials in the treatment of thyroid toxicosis, which is not a malignant disease in the cardinogenic sense, raises of course, a good deal of question as to whether this is a useful technique.

As far as the use of radioactive materials, including radioiodine in diagnosis, is concerned, the doses are very much smaller here, and with the use of I-123, the doses now are down to the point where the thyroid gland, which receives the bulk of the dose, may be expected not to, within our present knowledge, create great problems 20 or 30 years from now.

As far as the whole body dose, which is something you were concerned about with the previous witnesses, Dr. Kennedy and Mr. Villforth, the whole body dose here is extremely small, comparable to the doses that occur in diagnostic X-ray work.

So, sure, they have to concern us and again, this is the kind of commonsense regulatory activity that needs to be undertaken.

Mr. CARTER. We have had 600,000 people treated with radioactive iodine since 1942. Do you think we should have a study to determine what has occurred to those people, to see if they have developed diseases?

Dr. MORGAN. Certainly, Dr. Carter, enough time has now elapsed from the time of the first patients who were so exposed. This is over 30 years. Since a sizable length of time must elapse before the undesirable effects possibly occur, it would seem more than appropriate to take a look at this population.

Mr. CARTER. What can we do here as representatives of the people to lessen the hazards of radiation and to work with physicians who are using X-rays so that they will not overuse them?

Dr. MORGAN. There is a bit of question about the overuse of X-rays, and this has been primarily aimed at the diagnostic uses of X-rays, and certainly there has to be surveillance of this on a continuing basis. You can't do it in 1970 or 1963 and hope for the best in between. Fortunately, in diagnostic radiology, we have one or two things going for us that tend to keep radiation doses more or less automatically restricted, regardless of how unwise the medical profession or how lax the regulatory agencies may be? Every X-ray film takes a specific amount of radiation to produce a good film. It isn't higher tomorrow than it is today. It isn't lower the day after. It is a specific amount. Fortunately, that very fact causes to exist a control on the amount of radiation delivered per film exposed.

Now, where do you get into trouble with this? You get into trouble if a referring physician gets overly enthusiastic and orders a whole series of X-ray procedures or if a patient finds himself subjected to a whole series of repeated procedures because he goes to a number of hospitals for his care.

His physician may have X-ray equipment and undertake a number of X-ray studies. The physician then decides to put him in the hospital. The consulting physician may want some more studies of the same sort, not having access, perhaps, immediately to the original ones. The patient goes on then because he has a complicated illness to a referral center, a teaching hospital, such as our own, for example, and another set is taken.

Here, I think, there is a reason and cause for concern. And, you know, there isn't any reason other than the difficulties of transmittal of materials or the, I am sorry to say, perhaps a little laziness and perhaps a great deal of laziness on the part of the interested parties, that these repeated procedures are performed.

They are undesirable from the standpoint of radiation hazard which, I think, is perhaps the least of the problems. I think a larger difficulty here is the duplication of expense which tends to drive up all other costs all the way along the line.

Interestingly, when you find this problem with repeated radiological films and examinations, the chances are you will find that all of the other proedures, such as laboratory procedures, are duplicated too, which, again, run up the cost unnecessarily.

You have asked the question—I think it was you, Mr. Chairman—as to what the number of unnecessary examinations performed might be. I haven't the slightest idea, and I don't think anybody else has a good answer to this question. The numbers that have been cited, the 30-percent figure, was pulled out of the hat, I am sure, by somebody with inadequate information. I would hope that it is less than 30 percent.

My hope that it is less than 30 percent is because of the excess cost overusage entails reflection of medical overuse in general. And I would be concerned more about that than I am with excessive radiation exposure.

If the radiation exposure the population is receiving from medical sources were, on average, 10 times natural background radiation, then I would be very concerned. The fact that it is equal to or perhaps slightly less than natural background sources, to which everyone has been exposed since time immemorial, the problem obviously is less. And that is why I am more concerned about excess medical costs than I am about excess radiation exposure, although in emphasizing this point, I don't want to be misunderstood that radiation exposure is inconsequential. On the contrary, it is. So this fact that each film requires a specific amount of exposure puts a brake upon radiation exposure in medical practice, even though the number of films and the number of repetitious examinations is something which only the medical profession itself, I think, can address. It can be talked to ad infinitum by regulatory people, but I think here is a case where the medical profession must police itself.

I think, Mr. Chairman, you have a good point when you indicated that the Federal Establishment, not only the executive branch but also the legislative branch, might do a considerable service to everyone by bringing all kinds of costs—radiation exposure, dollar costs, the whole gamut—down to more reasonable levels.

Mr. CARTER. Just one or two short questions, Mr. Chairman.

As you know, the technique of X-raying people has been simplified in the last few years, and there have been improvements in film development. So one would think that 30 percent is a rather high rate of bad films; wouldn't you?

Dr. MORGAN. I think the percentage rate of bad films is very substantially less than 30 percent. In the 30-percent figure I think you have to include lots of other things than technical difficulties. Our experience, my own personal experience which, in this instance, covers a rather broad spectrum of interpreting chest films for the Department of Labor and for the National Institute of Occupational Safety and Health in the black lung program, the percentage has been consistently running, over the years, somewhere between 10 and 11 percent.

We very recently looked at these figures, and I give you figures not that apply back to 1970; they apply to 1978.

Mr. CARTER. I remember a time when we would have to go through three steps: first the developer, then the washing fluid, and then the fixer, and so on. Now it is a matter of 1 minute while the film is developed.

What do you think of taking X-ray films routinely such as chest films?

Dr. MORGAN. Getting back to commonsense and, as you say, there seems to be no great proliferation of this throughout the world, there is a time-honored axiom that I think is fundamentally sound and that is, you only X-ray people routinely who are at high risk. Hence, you don't X-ray people routinely any more for tuberculosis because the number of people at risk in the general population is vanishingly small.

There are some groups that conceivably deserve attention from health authorities, but I am afraid I am a nihilist when it comes to routinely doing anything. There just isn't very much evidence to indicate the existence of many disease processes that are helped significantly by early diagnosis. A lot of my colleagues will disagree with a generalization of this sort, and I will have to qualify it. Obviously, early diagnosis in cancer may be an important thing. Unfortunately, most of the technologies that we have, including radiology, are not very good at picking up very early neoplastic disease.

As you know, neoplastic disease falls into two or three general categories. There is neoplastic disease which, right from the word go, spreads rapidly so that early detection isn't going to help very much. Then there are those cases which are slow going, including many carcinomas of the breast. How many of you have seen women who have had a carcinoma of the breast removed, and who for 30 years have no evidence of disease. The original lesion was fortunately slow growing and the results were good regardless of whether the diagnosis was made at a particularly early time.

What routine procedure is going to help you in that sort of a situation? So by and large, routine X-ray procedures leave me very cold.

Fortunately, very few hospitals take routine chest films any more. This is one expense that has been avoided.

Mr. CARTER. Doctor, I want to thank you for your testimony. It has been very good, and I constantly renew what little I know medically in talking with gentlemen like you. A commonsense thing; it is a rare commodity. I give money to three different colleges for awards to youngsters who show the most commonsense.

Thank you, sir.

Thank you, Mr. Chairman.

Mr. ROGERS. I am glad you don't give those awards up here.

Mr. CARTER. I would have to give you one, Mr. Chairman.

Mr. ROGERS. I might say, too, we are pleased to see our former colleague here, Mr. Rutherford, who was a distinguished member of the Congress for many years.

Doctor, let me ask you this: Don't you think it would be well for us to work out some system with the Food and Drug Administration so that whenever they have a significant problem like the pelvimetry issue, they could call together those who should be concerned. They could let the college know, let the AMA know, have the state director or the State associations come in or have your own specialties come in for a meeting and really get these points across.

Dr. MORGAN. Yes. I am disappointed that good data aren't available on this because I suspect one will find, if one had good data, that this problem may have been a serious one in 1970, which is the last date——

Mr. ROGERS. But it has changed.

Dr. MORGAN. But there has been enormous change as a result of the replacement of X-ray methods with ultrasound, which is a nonionizing process. I know we don't do any pelvimetry in our hospital anymore.

Mr. ROGERS. They were doing it quite a bit, for instance, at the University of Washington, you recall, and then they did a study and were able to cut it down some.

Dr. MORGAN. Right. And it has been dropping.

Mr. ROGERS. So it seems to me they could call a quick national conference and get this type of information out quickly to the various medical centers.

I presume you would agree we probably are not doing a proper job of educating in the medical schools as to the results of radiation exposure. Would you say that is probably true?

Dr. MORGAN. I think it was more true 10 years ago, and to a less extent, 5 years ago. But yes, it is even true today.

You know, medical schools, perhaps with the help of people like many of us here and with the help of Congress, have received enormous amounts of money in recent years supporting medical research and great gains in may respects have resulted. But this has tended to create an ambiance in medical schools where all that seems to be important to a student is knowing what the latest things are that may be coming out of the laboratory. The mudane things don't get much attention.

I must say for may own medical school, there isn't an adequate amount of coverage of this subject. And you know, it wouldn't take very much, because it is a common sense process. But I will say this: that never before have I seen our medical students so aware of quasi-sociological issues, and I would classify excessive radiation exposure of the public as a quasi-sociological problem. They are much more aware than they have been in the past.

A member of your committee comes from our medical school. I know he reflects this changing attitude. I am glad to see it.

Mr. ROGERS. What does the American College of Radiology do to improve medical education?

Dr. MORGAN. It has a great many educational processes going on continuously.

Mr. ROGERS. In other words, where you see something being done that you think could be changed, do you contact the colleges?

Dr. MORGAN. Yes.

Mr. ROGERS. That is done?

Dr. MORGAN. Yes.

Mr. ROGERS. Maybe you could set forth for the record, not now, generally———

Mr. LINTON. It is in our testimony.

Mr. ROGERS. Fine.

Do you have any program of research or development directed at improving the technology of diagnostic X-rays?

Dr. MORGAN. The College itself, of course, is not organized to do research.

Mr. ROGERS. I wondered if you sponsored———

Dr. MORGAN. But its members certainly are. That, perhaps, gives me an opportunity to just say the College has been having discussions with Dr. Fredrickson and Dr. Malone in the National Institutes of Health about increasing the support for radiological research at all levels. Currently, if you look at the statistics—and we will be glad to———

Mr. ROGERS. Furnish those for the record?

Dr. MORGAN. I don't think these are in the record, but we will dig them out for you.

The statistics indicate that the current support for radiological research in the health agencies is dismally low.

[The information requested was not available to the subcommittee at the time of printing.]

Mr. ROGERS. That is my impression.

I think the committee would like to be helpful there, too, I would agree.

Dr. MORGAN. Sorry for interrupting. This is why we are so concerned about the lack or absence of a focus for radiation research in the Federal establishment.

Mr. ROGERS. I agree.

The President has just issued a statement directing the Department of HEW to be a lead agency in trying to make determinations on health research effects. I think that is a good step forward. As a matter of fact, this committee requested that action.

Dr. MORGAN. Very good.

Mr. ROGERS. It is beginning to move. Now we do need to bring some focus in, I think, without question.

Now let me ask you this: Do radiologists actually make a judgment as to whether an X-ray is needed? Suppose a physician or surgeon says take a picture of so and so. Suppose the radiologist says, Why is he doing this? I don't think that is going to get him much information. Is the tendency just to go ahead and do it? We had one radiologist tell us when he didn't do it; then he had his income cut about a third.

Dr. MORGAN. In addition to cutting his income, I suspect he also brought down the wrath of his associates to some extent.

Mr. ROGERS. But shouldn't the radiologist make these judgments?

Dr. MORGAN. Yes. And I think the situation which exists today is a reflection of the way in which radiology has been practiced over the last 40, 50 and more years. The radiologist on the record should seem to be a consulting physician. If I am a general practitioner or an internist and I have a patient whom I want a neurologist to come and see, I would no more think of laying down any rules to that neurologist in practicing on that patient. When I ask him to come in as a consultant, basically I turn the patient over to him, and until he gives me his report, he is perfectly free to determine the procedures that he will perform.

Not so in radiology. The radiologist has often been regarded as only providing a service. Now as the radiologist has become more clinical—gotten himself into situations where he is more clinically involved, such as in cardiac catheterization for the diagnosis of various heart problems or involved in the diagnosis of brain conditions, neuroradiological procedures—he has played more and more the role of consultant who does determine what shall be done and what shouldn't be done. And fortunately, I think the situation is going to spread.

Mr. ROGERS. What could we do to encourage that, because it appears-and from the testimony we have—that should be a proper function for the radiologist.

Dr. MORGAN. Yes, indeed.

Mr. ROGERS. Should it be attached to medicare-medicaid as a requirement that the approval of the radiologist also must be given before X-rays would be paid for?

Dr. MORGAN. I think there is something more than that, Mr. Chairman, that is needed.

Mr. ROGERS. I just thought as a quick-driving force.

Dr. MORGAN. I think this may be useful for the interim, but I think the radiologist has to become much more a clinician than a simple reader of films.

Now fortunately, there is something coming along which I think is going to help us a great deal. We have not mentioned it yet, but you have heard testimony on CT scanners, sometimes called CAT scanners, and most of the time these have been decried as being terribly expensive devices.

Mr. ROGERS. Well, our cost containment bill, I must say, has gotten the price down. They are now under $150,000, which is the cut-off level for approval. So maybe the bill has some advantage.

Dr. MORGAN. Exactly.

Now, CT scanning requires the radiologist to become very much more involved in the clinical diagnosis of disease and its ultimate care; that is, CT scannng requires the radiologist to become much more than a film reader.

There are many reasons for this, and I don't propose to go into them here because the hour is late. But CT scanning should be recognized as a technique that is likely to cause major changes in the way radiologists practice medicine. Ten years from now, the fundamental units needed to set up an X-ray department in a traditional hospital will not include a lot of very complicated X-ray apparatus.

Instead, there will be three basic elements: (1) a chest unit, because 45 to 50 percent of all examinationas done are of the chest, (2) a general purpose radiographic fluroscopic table, in which you can do such things as barium enemas, GI series, and the like, and (3) a CT scanner.

Whenever I say this to Hospital Service Cost Review Commissions, they become very concerned because of scanner costs. However, it is very, very difficult, Mr. Chairman, for me to overstate the great role that CT scanning will assume in medicine in the future—a role that will require radiologists to become full fledged clinicians.

Mr. ROGERS. May I say, I understand the importance of the CAT scanner, and we don't want to reduce their proper use, and I don't think we should because I think that what will happen, as the profession becomes more comfortable with the technology and knows how to use it and depend upon it, it then no longer becomes cumulative, which is the present problem because we take all the X-rays plus the CAT scanner and everything else. As we get more comfortable with the knowledge, then I understand the cost will reduce and we won't be doing the duplicative work.

Dr. MORGAN. And hopefully the mass production of these devices will bring their cost down.

Mr. ROGERS. Cost is being brought down already.

Dr. MORGAN. Since most of the cost is in semiconductors and computing equipment, we know that the costs of these are coming down and this is all good.

Mr. ROGERS. May I ask—and I presume that is so from the previous statement, but I assume the College would work closely with the Food and Drug Administration if they wanted to call a conference.

Dr. MORGAN. By all means.

As a matter of fact, we have contracts with them now. We work very well with them.

Mr. ROGERS. Thank you for your presence. Thank you for the advice you have given to the committee. It has been most helpful, and thank you for your patience.

The committee stands adjourned until 2 o'clock tomorrow afternoon.

Thank you.

[Whereupon, at 5:55 p.m., the subcommittee adjourned, to reconvene Thursday, July 13, at 2 p.m.]

EFFECT OF RADIATION ON HUMAN HEALTH

Radiation Health Effects of Medical and Diagnostic X-Rays

THURSDAY, JULY 13, 1978

House of Representatives,
Subcommittee on Health and the Environment,
Committee on Interstate and Foreign Commerce,
Washington, D.C.

The subcommittee met, pursuant to notice, at 2:20 p.m., in room 2322 Rayburn House Office Building, Hon. Paul G. Rogers, chairman, presiding.

Mr. Rogers. The subcommittee will come to order, please.

This afternoon we are continuing our oversight hearings on radiation health effects of medical and dental diagnostic X-rays. We are very pleased this afternoon to have the chairwoman of the Conference of Radiation Control Program Directors and chief of the section of radiation control of the Minnesota Department of Health, Ms. Alice Dolezal.

We are very pleased to have you with us. I want to express the appreciation of the committee to you for being here.

Your statement will be made a part of the record in full, and you may proceed as you desire.

If you could highlight your statement, it would be helpful.

STATEMENT OF ALICE DOLEZAL, CHAIRWOMAN, CONFERENCE OF RADIATION CONTROL PROGRAM DIRECTORS

Ms. Dolezal. Thank you, Congressman Rogers.

I am Alice Dolezal of the section of radiation control for the State of Minnesota. I am here today speaking as chairwoman of the Conference of Radiation Control Program Directors, an organization whose membership comprises the directors of radiation control for all the 50 States and certain territories and large municipal agencies.

The conference is pleased to have been asked to testify on this very vital subject in controlling diagnostic X-ray use.

Mr. Chairman, I have submitted written testimony for the record. Since the written testimony is too lengthy to read, I will highlight some areas in the testimony presented here. There are certain key issues on which we would like to present testimony.

To understand the concerns of the conference and its role in relation to State radiation control programs, a brief history may be helpful.

The Conference of Radiation Control Program Directors was formed approximately 10 years ago as a forum for the exchange of radiation health and safety information between the States and Federal agencies as well as among States. The conference is supported by several Federal agencies: the Food and Drug Administration, Environmental Protection Agency, and Nuclear Regulatory Commission.

We also have projects with the National Bureau of Standards and have liaison with a number of different Federal departments, including the Department of Labor, Department of Transportation, and groups such as the National Governor's Council, the American College of Radiology, the Health Physics Society, and ANSI, the American National Standards Institute.

The goal of the conference is to insure that the patient who is to receive either diagnostic or therapeutic radiation, the worker in radiation, the consumer and the general public at large receive the least amount of radiation exposure consistent with the benefit to be derived.

The expressed purpose of the conference to serve as a forum for the exchange of ideas prompted us to form task forces to evaluate, discuss, and subsequently recommend specific actions for problems that have been identified. These task forces have not only State members but Federal representatives and industry and professional group representatives.

I have, as part of the written testimony, submitted two of the draft task force reports, "Healing Arts X-Ray Control Program Criteria," [see p. 549] and "Quality Assurance in Diagnostic Radiology."

Mr. ROGERS. We will receive those, without objection, for the record.

Ms. DOLEZAL. In conversations with the staff, I understand you wish to restrict the hearing today to the healing arts use of X-rays, and we will do so.

As part of the written testimony we have submitted copies of the proceedings from three annual meetings. Rather than taking the proceedings from each of the annual meetings, we have chosen the last three: the seventh, eighth and ninth annual meetings. These will highlight the issues and problems identified and the actions taken to resolve them.

Before moving to specific issues relating to the healing arts, the historical State government involvement may be pertinent. State radiation control programs developed in the early 1950's. They began with Federal support in model legislation, grant funding and training programs for the states. The attention was concentrated in the areas of X-ray use and occupational exposure.

Concurrently, the radioactive materials control was investigated, and in 1959, Congress amended the Atomic Energy Act by permitting the States to participate in the control part of the by-product sources and special-nuclear material. The amendment permitted such participation by the process of becoming an agreement State.

With these two separate but timely beginnings, States have continued to accept more and more responsibility for radiation protection programs. As of February 1978, 48 States, Puerto Rico and the District of Columbia had laws for regulatory programs in ionizing radiation control; 14 States and Puerto Rico had enabling legislation for credentialing of the user of X-ray; 5 States and Puerto Rico had implemented credentialing programs; 26 States have specific statutes for control of non-ionizing radiation; 25 States had signed agreements and become NRC agreement States.

The total State commitment in fiscal 1977 was over $12 million and approximately 530 person years.

Through these programs, over 23,000 dental X-ray units and over 23,000 medical X-ray units per year have been inspected. Information is not yet available for the numbers of inspection of radioactive materials, non-ionizing radiation devices and special studies on training of users conducted in fiscal 1978.

As these areas indicate, States become involved in a variety of efforts to improve radiation protection.

A more detailed analysis of State efforts may be found in the document entitled "Report of State and Local Radiological Health Programs" for the year 1976, published by FDA. There is a copy of the document in the written testimony.

Mr. **Rogers.** Thank you.

Ms. **Dolezal.** The fiscal year 1977 publication will be available probably in a few weeks.

With that background, Mr. Chairman, I would like to go on to discuss some of the issues the Conference believes necessary to be addressed for effective control of X-rays. Only those issues that involve radiation producing devices will be discussed.

It must be noted that States rarely, if ever, have the personnel, money or administrative structure to divide radiation protection among a large variety of agencies, bureaus, commissions, departments, and committees such as is the current Federal practice. The number of separate Federal agencies which impact on the State program is itself an issue.

This has been described in the Conference resolution dated May 1973 and reconfirmed in a letter dated May 19, 1978, in response to a request from Senators Ribicoff and Glenn. A copy of this letter is included with the written testimony. [See p. 565.]

The isolation of issues involving radiation-producing devices, as defined in Public Law 90-602, may distort the view of the problems encountered by the State because these devices comprise just one portion of the radiation control program. Examining only those issues identified with healing arts X-ray may provide the subcommittee with an erroneous impression of the variety of areas encompassed by the State program.

Among the key issues listed by Mr. Charles Hardin of Kentucky, representing the Conference in testimony before the Senate Committee on Commerce, Science and Transportation on June 29, 1977, is the reduction of unnecessary radiation exposure from X-rays in healing arts.

Mr. Hardin listed as contributing factors: Inadequate training in radiation protection by both operators of sources and nonradiologist practitioners, nonefficacious use of X-ray sources, inadequate quality control programs in X-ray facilities resulting in retakes of radiographs, and improperly designed X-ray systems.

An area identified relating to use of radiation-producing devices in healing arts is the reduction of unnecessary radiation to radiation workers. It is especially important in relation to the exposures encountered in the use of medical fluoroscopy. The Conference considers all of these issues as still currently vital.

A few points should be made in regard to these issues. Note the use of the term "unnecessary exposure." Use of this term is derived from two factors. First, for estimating radiation effects in humans, the current national accepted view is that it is a reasonable to assume nonthreshold, linear, and proportional dose-effective relationship; and second, it is necessary to balance even the small risk against the benefit derived.

One should speak of reducing, inasmuch as is practical, any exposure which derives no benefit; that is, unnecessary exposure rather, than monitoring risks, reducing hazards, or counting lives saved. Reducing unnecessary exposure may, indeed, save lives, but sampling constraints, data collection, limitations, and the nature of ionizing radiation exposure effect relationships, prohibit individual States singly or as a group from identifying any specific life that has been saved or even predicting the number of lives that were saved by a particular program. Such computations are left to academia, the Federal Government and those whose have resources and interests can best be applied to such studies.

Factors contributing to unnecessary radiation exposure in healing arts should be discussed further. For example, one factor identified as contributing to unnecessary exposure was improperly designed X-ray systems. It should be noted that the States inspect systems designed both before and subsequent to the effective date of the certification requirements pursuant to Public Law 90-602. Therefore, the identification of an improperly designed system may or may not reflect upon the effectiveness of the certification standards since the number of certified machines inspected per year is less than 4 percent of the total number of systems being used. The number of certified systems available for inspection is less than 20 percent of the total number of installed systems.

Another factor identified as contributing to unnecessary exposure is inadequate quality control programs for X-ray facilities. Programs have been and are being developed to meet that need, but until such programs have time to function, continued unnecessary exposure should be expected.

I would now like to address several additional topics which were identified in my discussion with Mr. Connolly and other staff members as being of interest to this committee. These topics include risks from diagnostic X-rays, uses of X-rays, and control of X-ray.

As indicated before, the radiobiological risks require a regulatory position that assumes some risk with any exposure and demand reduction of unnecessary exposure. The States' occupational exposure limits are not intended to imply complete safety below or unavoidable damage above. They are legal benchmarks, or points of reference. The ideal radiation-control program monitors the exposures of radiation workers and the public and achieves needed corrections by means of education, consultation, or regulatory sanctions to bring the exposure to the lowest practical level. Many States also measure patient exposure and consult with the users.

Reductions in exposure have been achieved using this consultative approach. The Breast Exposure: National Trends, or BENT program, is an example of a program jointly operated by the States and the FDA Bureau of Radiological Health that has achieved very satisfying reductions in exposure while improving film quality using essentially a voluntary, consultative approach. Measurements of effectiveness of such programs is very difficult due to the rapid change in the program while requirements that attempt to measure the impact also change.

In addition, it is usually not possible statistically to count real radiation injuries, especially those from delayed somatic injury, and indirect measures must rely on parameters, which can change; therefore, effectiveness has been very difficult to demonstrate.

It has been noted that between 1964 and 1970, the genetic significant dose, as measured and computed by FDA, did not change significantly in spite of a sharp increase in X-ray use. It is hoped that this represents, at least in part, the efforts of the States and their Federal associates, because if the genetic dose followed the use curve, it would also have increased sharply.

From the issues identified previously, additional programs may evolve. Based on the need to reduce unnecessary exposure, we would propose:

First, training for both State personnel and users. The means providing for such training for users suggested by the Conference involves certification. One excellent recent development for staff training is the FDA video network, through which every State radiation control program has access to video tapes, the tape player, and television. Some video tapes have been provided already, and I would recommend expansion of this effort.

Second, clarification of current Federal standards which may contribute to the use of X-rays to meet Federal standards rather than diagnose the patients. Some of these Federal standards are in OSHA's requirements and also medicare, medicaid and other Federal requirements. Some of these appear to be of dubious benefit to the patient.

Third, develop a working relationship with every State whereby the number of inspections of certified systems can be increased to provide more meaningful data and permit more rapid corrections where needed. Meaningful, in this context, signifies that State inspectors and inspection reports concentrate on important system components such as the filtration or the beam limitation rather than labeling.

And fourth, that inspections mandated as a result of Public Law 90-602 be financed from Federal, not State, funds.

It should be clear, from the previous discussion, that unnecessary exposure to X-ray is perceived to be a problem by the Conference. There are many causes for unnecessary exposure, and only a portion of them can be addressed by the Conference or the States' radiation control programs.

Some of these causes have already been identified. There are others toward which the Conference efforts will necessarily be indirect, including improvement of patient selection criteria, limiting of X-rays to patient diagnosis, not medical legal proofs of quality care, and third, patient education to decrease self-prescribed or unnecessary X-rays.

We will rely, in large measure, upon the work being done by the American College of Radiology, FDA, and EPA in standards development for guidance in these areas. The Conference currently has a task force devoted to investigating efficacy and the criteria for determining it.

Reduction of unnecessary radiation exposure can sometimes be best achieved when responsible agencies cooperate to pursue a common goal. An example of a type of cooperative approach could be the development by FDA, the professional societies, and the Conference, of model legislation and regulations for X-ray technologist certification.

We are aware of no such models which enjoy the full support of all parties. The Conference has expressed on two separate occasions, via resolutions passed in 1971 and 1974, support for the concept of technologist certification as a means to upgrade training in radiation protection. Copies of these resolutions are included in the written testimony.

My previous testimony discussing the risks and uses of X-rays described relevant areas of the radiation control program. Risk and uses cannot logically be separated from control program. My intention has been to describe the risk and related means by which the program must be designed to be compatible with it.

Similarly, management of X-rays use through control program operations has also been mentioned. It might be clearer to indicate that the Conference recognizes that the control of radiation requires input from a number of different sources, including States, Federal Government, physicians, physicians' professional associations, manufacturers, assemblers, and the public.

Each of these organizations has a unique contribution to make, and the Conference would encourage each to make that contribution early and often. If we work together in a cooperative professional manner, we can improve the use of X-rays and reduce unnecessary exposures, thereby preserving a very powerful tool for diagnosis and treatment of disease and injury without administering unnecessary radiation to the public.

Thank you for providing the Conference with the opportunity to speak to you today on this vital issue.

I did receive the list of questions on this topic last week, too late for response to be provided today. But written response will be provided soon.

[Testimony resumes on p. 569.]

[Healing arts X-ray control program criteria and letter to Senators Ribicoff and Glenn follow. The other reports and document referred to by Ms. Dolezal may be found in the subcommittee files.]

HEALING ARTS X-RAY CONTROL PROGRAM CRITERIA

APPENDIX 1

I. Legislation and Regulations

a. The State should have enabling legislation and regulations essentially in conformity with the Council of State Governments suggested legislation and regulations, including authority to enter into interstate and Federal-State arrangements for the control of radiation hazards. Legislation and/or regulations should contain provisions for reciprocity with other States and coverage of x radiation used in the healing arts.

b. At least every 5 years, regulations should be critically reviewed and updated as necessary. The appropriate healing arts groups should be provided an opportunity to review and comment on proposed changes.

II. Personnel

a. State radiation control x-ray program personnel should be qualified by training and experience in the field of x-ray hazards and control. Inspection personnel should include qualified college graduates and/or technicians having completed a minimum of a two-year formal technology program in radiation control, or the equivalent.

b. Personnel for the x-ray control program should number at least 3 full time equivalents/1000 tubes. (See appendix 1 for documentation.)

c. The State should have specifications for professional employees functioning in the x-ray control field.

d. Each State professional employee should have an accurate, up-to-date description of his position, detailing specific responsibilities and authority.

e. It should be possible for any professional entering the system to progress through the various levels up to and including radiation control director.

f. Over a 3 year period, there should not be greater than a 50% turnover in personnel inspecting x-ray machines, except for promotions or transfers within the radiation control program. (A high turnover rate is generally indicative of problems.)

III. Training

a. On-the-Job Training

A specific program should be established for on-the-job training of new employees by supervisory and senior personnel. New employees should be provided with the State regulations and written registration, inspection, and compliance programs for review.

b. In-service Training

The state radiation control program should have a planned continuing program of in-service training consisting of seminars, demonstrations, lectures by consultants, short and long term training, attendance at professional meetings (Health Physics Society, etc.), to keep personnel abreast of current developments in the control of radiation hazards.

a. The state should have a records and statistical system which includes the following components:

1. a continuing integrated registration program.

2. physical survey forms containing minimum uniform data and compliance and enforcement actions.

3. data accurately and rapidly retrievable,

4. radiation control employee personnel monitoring results,

5. fiscal and other administrative records,

6. records of machine transfers and vendor notification,

7. records of incidents and investigations.

b. The State should utilize the above records in

1. program planning and evaluation, and

2. carrying out field survey and inspection programs

c. The State should make maximum use of available electronic data processing facilities. (See appendix II for a description of a suitable record keeping system.)

V. Program Organization

a. Ideally all State radiation control activities should be located in the same agency.

b. Radiation Advisory Committees

The program should have a radiation advisory committee that is established to provide, as a part of its function, guidance and assistance on nonroutine, medical applications and to advise on the use of x radiation in the healing arts.

VI. Program Planning and Evaluation

Each State should have a written plan of action describing present and future program activities. The plan should include the following basic components:

1. Problem

In defining the problem the State should include the extent, nature of the radiation exposures involved and, in so far as possible, the poulation affected.

2. Objectives

The State plan should set forth both long- and short-term objectives. Based on current and anticipated resources, target dates should be established for priority projects.

3. Methodology

The State plan should describe those activities directed to fulfill stated objectives.

4. Evaluation

The plan should include a method of evaluating (involving the establishment of criteria) the progress of the State programs. Important components of the State evaluation program should include an assessment of the radiation hazards and population affected for setting priorities.

VII. Public Information and Education

a. The State should maintain liaison with professional groups leading to seminars, training courses, and public documents or radiation control.

b. The State should provide x-ray registrants with current reference material, guidelines, and standards as they are available.

c. The State x-ray control program should seek opportunities to inform the public of program activities (i.e. through newspaper articles, TV, radio, incidents, etc.).

VIII. Special Studies

State Radiation control programs should have sufficient personnel, fiscal support, appropriate instrumentation, and initiative to undertake special studies including x-ray protection, e.g. identify new problems that need investigation, develop more efficient procedures and methodology, andcooperate with Conference and/or federal programs.

IX. Equipment

Field x-ray equipment and instrumentation should be capable of detecting and measuring x-radiation exposure to determine compliance with applicable guides and regulations and to provide estimates of radiation doses to patients, operating personnel, and the general public.

The State x-ray control program should be capable of providing and servicing of all x-ray equipment and instrumentation.

1. Ideally, a survey kit should be provided for each FTE in the field. (Refer to the Optimum Survey Procedures Manual for a partial listing of the equipment, materials, and supplies that can be useful to the field inspector. However, special equipment may be needed for special studies. For example, low energy detectors will be necessary for evaluating mammography equipment and high energy detectors will be necessary for certain therapy equipment.)

2. There should be a system for calibration and servicing of each radiation detection instrument on a planned schedule. The schedule should call for

an annual calibration with calibration checks performed on a quarterly basis. Calibrations may be done by the State radiation control program using its own calibration source, equipment, and procedures, or by a commercial instrument calibration and repair service under contract. Such calibration and servicing should be the responsibility of one member of the program staff. Each instrument should bear a tag stating the latest date of servicing and calibration, and a calibration curve or correction factors for each detection range.

X. Registration, Inspection and Enforcement

a. The State should have authority to register x-ray sources. Part B of the Council of State Governments Suggested State Regulations for radiation control may be used as a guide in developing the extent of the registration function.

b. Inspection

A State should conduct its own inspections, obtain survey reports from qualified private consultants or from radiation safety officers employed by the owner of an x-ray installation, or a combination of these approaches.

The qualifications for private consultants or radiation safety officers should be established when the survey reports by such individuals are used by the State to evaluate continuing compliance with its standards or recommendations.

1. Inspection Procedures

The State should have written inspection procedures to insure that uniform inspections are conducted and these procedures should be available as a guide to the inspector while in the field. The Optimum Survey Procedures Manual can be used as a reference to develop these written procedures.

2. Inspection Schedule

A periodic inspection schedule should be established. An example of such a schedule is as follows.

a.	Dental x-ray machines	- every 5
b.	Medical x-ray machines	- every 2 years
c.	Hospital or similar facility	- every year
d.	Clinic (radiologist)	- every year
e.	Chiropractors	- every year
f.	Osteopaths	- every 2 years
g.	Veterinarians	- every 2 years

c. The State should establish written enforcement procedures. Such procedures should detail the steps to be taken within a specified time period to accomplish compliance with the regulations (See appendix 2). In addition, interpretations based on policy decisions should be accumulated and maintained to ensure consistent enforcement policy.

XI. User Education

a. A uniform, minimum level of training in radiological health for all operators of x-radiation machines should be established.

b. The State should encourage, sponsor, or conduct continuing, formal education programs for users or operators of x-ray sources.

c. The inspector should take advantage of his time in x-ray facilities to educate, assist, and answer questions regarding radiation safety and good radiological practices.

XII. Quality Assurance

The State should have a plan to encourage and assist registrants in establishing quality assurance programs to ensure that all images are of a consistent high diagnostic quality and that all treatments are properly administered.

APPENDIX 2

An X-Ray Program Recordkeeping System

A. Registration:

1. On receipt of an application: (See Attachment 1)

   a. Check to assure that applicant has not previously been registered. The installation and not the specific x-ray unit is registered.

   b. If not registered, obtain new registration number, county-discipline-sequential.

   c. Complete registration certificate (See Attachment 2) with three carbons and send original to applicant.

2. Initiate Folder:

   a. Place application form and first carbon copy of the registration certificate in the folder. Add any other correspondence concerning this registration. File by sequence number.

3. Place second carbon copy of the registration certificate in the sequential file.

4. File the third copy in the current county file to be surveyed.

5. Two index cards (4x6) will be completed. On these cards will be the name and address of the registrant and the registration numbers. File by alphabetical discipline order and county.

B. Change in Registration:

1. State address change:

   a. Whenever a registrant moves from one county to another, a new certificate will be issued. Follow registration procedure.

   b. Whenever a registrant moves to a new location within the same county, no new certificate will be issued. Only change address on the present certificate, and flag for resurvey.

2. Out-of-State address change:

   a. Whenever a registrant moves out-of-state, the registration certificate will be flagged inactive and will indicate the move. The alphabetical discipline and county index cards will so indicate and be moved to the inactive status. The registration numbers will not be reissued.

3. Deaths or Retirements:

    a. Whenever a registrant dies, or retires, the registration certificate will be flagged inactive and will indicate the death or retirement. The alphabetical discipline and county index cards will so indicate and be moved to the inactive status. The registration numbers will not be reissued.

    b. After a six (6) month period, a phone call to the retiree or widow will be made to determine status of the machine. Record information accordingly.

C. Survey Forms and Results Sheets:

1. After an inspection, Survey report forms (See Attachments 3, 4,5,6, and 7) will be completed, data processed, and filed in the sequence folder.

2. Also, after an inspection, survey result forms (see Attachments 8,9, and 10) with one carbon copy will be completed. The original will be left with the registrant, and the carbon is returned to the office for filing in the sequence folder.

3. No further action will be taken on facilities in compliance with the regulations.

D. Non-Compliance Survey Reports:

1. As noted on bottom of survey results form, the applicant has sixty (60) days to correct items of non-compliance.

2. After an inspector returns to the office, he/she will complete a 3x5 white card with registration number, survey date, and remarks.

3. This card will be filed in the non-compliance post card file (placed behind month) 60 days from end of month in which inspection was made.

4. If the facility becomes "in compliance" before 60 day period has passed, destroy the 3x5 card.

5. At the end of each month, pull all 3x5 cards for that month.

6. Send post cards (See Attachment 11) to all appropriate non-compliances. Post 3x5 cards forward one additional month.

7. Returned post cards will be placed in sequence folder and 3x5 cards destroyed if in compliance.

8. If answer is not received in one month (30 days), a letter will be sent indicating inspection date, inspector, items of non-compliance, and that the applicant has 15 days to report corrective action taken.

9. If action is not reported within 15 days, a letter for the Health Officer's signature will be prepared.

10. If applicant does not respond, the case is then turned over to the Attorney General's office for handling.

E. When "Non-Compliance" Items Have Been Corrected:

1. Indications from any responsible person that items of non-compliance have been corrected will be accepted. For example:

   a. Phone calls from applicant or applicant's office.

   b. Returned post card.

   c. Call or letter from x-ray representative.

   d. Letter from applicant, etc.

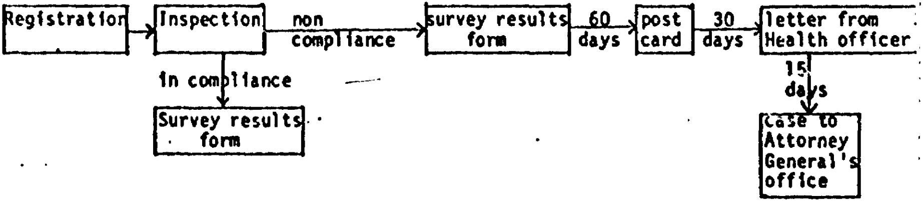
2. Upon receiving information the following will be done:

   a. Survey report form will be marked compliance by indicating date information was received and by what route.

   b. Survey result form will be marked compliance by indicating date information was received and by what route.

   c. Three by five card will be destroyed.

F. A simple flow chart of this system follows:



CONFERENCE OF RADIATION CONTROL PROGRAM DIRECTORS

Report of Task Force 2A

The following is submitted in response to a request from the Healing Arts Council to report on the activities of the Task Force.

CHARGE

Task Force 2, Part A was assigned the charge of developing criteria that can be used to evaluate the adequacy of a state x-ray and non-ionizing program. In carrying out this assignment, the Task Force was reminded to consider mechanisms that would ensure compatibility among Federal and State programs in the enforcement of radiation protection standards and regulations.

MEMBERSHIP

The Executive Committee appointed John Shaver, University of California at San Francisco as Chairman and Simon Kinsman, Past Chief of the California Radiologic Health Unit, and Jim Hickey, Rhode Island, as members. Richard Gross, Bureau of Radiological Health, and DeVaugh Nelson, Evironmental Protection Agency, were assigned a federal resource persons. Mr. Charles Showalter has met with the Task Force representing Mr. Gross. In addition, Bobby Dillard, FDA Region VII and Warren Jacobi, Colorado, have met with the Task Force during its only full meeting. Mr. Shaver and Dr. Kinsman met with Messrs. Morgan Seale and Dale Stevenson, FDA Region IX and Mr. Robert England, California, to obtain their views regarding this assignment.

MEETINGS

ıe Task Force met April 26-27, 1977 in Denver, Colorado. This report is based upon the results of that meeting. All members were present except Dr. Nelson and Mr. Gross who was represented by Mr. Showalter.

HISTORY

Workshop #1 at the 7th Annual Conference in Hyannis, Massachusetts was charged to consider the development of criteria for an adequate State Radiation Control Program. In its report to the Conference, it recommended the formation of a Task Force to further study this matter. In September, 1975, the Executive Committee implemented this recommendation by forming a Task Force; however, funds were not available for support. In September, 1976 the Executive Committee decided to reactivate the Task orce. In December, 1976 the charge was clarified and funds were allotted to hold four meetings. As reported above, the Task Force has held one meeting.

BACKGROUND

The problem of developing suitable program criteria has surfaced on numerous occasions and has been given considerable attention by the Bureau Radiological Health, Nuclear Regulatory Commission, and selected States. For example, in 1969 the BRH prepared a detailed questionnaire as part of a study to evaluate the status of state radiation control programs. The questionnaire was carefully developed with input from states, regional offices and other federal agencies such as the AEC. It was pilot tested in most regions, and revised and improved based upon those tests.

Other work in this area includes the sending of Federal and State survey teams upon request to selected states to conduct detailed Program evaluations. The Atomic Energy Commission has developed detailed criteria to evaluate Agreement States to ensure program compatability. In 1972, the Southern Interstate Nuclear Board conducted a study of Radiological Health Programs in the South. The Conference has formed workshops to consider this matter. The Task Force has taken full advantage of this previous work.

DECISIONS

Following a careful review of available materials, the Task Force decided the following:

1. The charge could be best implemented by developing a comprehensive list of criteria to be used by State Program Directors. The criteria should reflect the needs of a comprehensive program, should be detailed enough to assess staffing and funding needs, but flexible enough to account for the wide spectrum of individual state needs and resources.

2. Program Directors should compare their program with these criteria to determine deficiencies or weak areas. Upon identification of weaknesses, a Director can point to the deviation from nationally accepted criteria to add support to justifications for budget or legislative requests.

3. In developing the detailed criteria the Task Force would utilize to the maximum extent possible the information contained within the BRH publication entitled "A Study of Selected Aspects of State Control of Radiation Hazards."

BEST COPY AVAILABLE

4. The Task Force would not to develop criteria for non-ionizing radiation sources in that adequate control seems to exist at the federal level via the development and enforcement of performance standards. This decision will be restudied if so directed by the Conference.

RECOMMENDATIONS

1. The criteria should be distributed to each State Program Director and appropriate Federal agencies for evaluation and comment. Comments should be centrally received, collated, and the criteria appropriately revised.

2. The revised criteria should be presented to the Conference at its next annual meeting for acceptance and endorsement.

3. The Task Force is willing to act as the clearinghouse for receiving comments and revising the criteria. In this regard, funds should be alluted for one Task Force meeting to assemble the final criteria.

CONFERENCE OF RADIATION CONTROL PROGRAM DIRECTORS
717 Delaware Street Southeast, Minneapolis, Minnesota 55440
(612) 296-5323

May 15, 1978

Senator Abraham Ribicoff, Chairman
Senator John Glenn
Committee on Governmental Affairs
United States Senate
Washington, D.C. 20510

Dear Senators Ribicoff and Glenn:

In reference to your April 19, 1978, letter to Mr. J. Dale McHard, the 1977-78 Chairman of our Conference, requesting this organization's views on organizational issues concerning Federal radiation health and safety programs, the following is provided.

During the 5th Annual National Conference meeting in 1973, the following resolution was passed by the membership.

> "RESOLUTION ON CONSOLIDATION OF FEDERAL RADIATION AGENCIES
>
> WHEREAS the responsibility for the protection of the public and worker from exposure to radiation has been significantly fragmented at the Federal level; and
>
> WHEREAS this fragmentation of responsibility is divided among the Atomic Energy Commission, the Food and Drug Administration, the Environmental Protection Agency, the Department of Transportation, the Department of Labor, the Office of Emergency Preparedness; and
>
> WHEREAS this fragmentation is further exhibited between regional offices and headquarters offices with certain of these Federal agencies; and
>
> WHEREAS this fragmentation results in duplication, inefficiency, contradictions, and complexities in communication: Therefore,
>
> BE IT RESOLVED, that the Conference of Radiation Control Program Directors, urge the Congress of the United States to consider this serious problem of fragmentation and take the necessary legislative action to consolidate the various Federal responsibilities relating to radiation protection of the public and worker within one agency." (emphasis added)

BEST COPY AVAILABLE

This resolution was submitted to the President of the Senate, the Speaker of the House and the Joint Committee on Atomic Energy by the then Chairman of our Conference. During our 9th and 10th Annual Conference meetings in 1977 and 1978 respectively, this position of the Conference was reaffirmed by the membership. The Conference recognizes also that, because of various circumstances that Congress must address, this idealistic approach to the problem may be an unacceptable solution. With that concept in mind, the Conference is providing its comments and suggestions pursuant to your request.

The Conference fully concurs with the study's assessment that there definitely is a lack of central focus in the administration of the numerous Federal statutes in the field of radiation health and safety. Additionally, we thoroughly agree that there is a lack of coordination between the Federal Agencies having responsibilities in radiation protection.

The provision of separate and isolated efforts by several agencies in this field bring due criticisms from the public of inefficient and ineffective government, a situation which the Conference since its inception 10 years ago has strived continually to preclude.

Provision should be made for the development of Federal guidance for signature by the President which addresses the full spectrum of radiation protection including ionizing and non-ionizing radiation, and exposure of the worker, patient, the general public and the environment. This assignment of authority must be clearly defined and duly delegated. Assignment of this responsibility should not be made to an office of an agency which also has the responsibility for the implementation of such Federal guidance.

A mechanism should also be established to require coordination between Federal agencies having responsibilities for radiation protection. This coordination must originate at the top level of agency administration if such coordination is to be effective.

The recommendation that a "lead agency approach" be adopted, consistent with the statements in the final paragraph of Item E as found on page 339 of the Senate Governmental Affairs Committee Study Volume V, is found to be generally unacceptable. While EPA has several applicable statutes under its current jurisdiction, it cannot and should not usurp authorities provided under statutes not under its jurisdiction. EPA should also not be the sole authority over the Federal guidance development and the implementation of such guidance under its own regulatory functions. No Federal agency should be authority both to

BEST COPY AVAILABLE

develop the philosophical criteria (Federal guidance) and implement regulations under such criteria due to the possibility of conflict of interest considerations. Additionally, we feel that the "lead agency approach" similar to that contained in the Toxic Substances Control Act is inappropriate for this situation due to the enormity of the Federal radiation protection effort and that for the most part the Toxic Substance Control Act has not been implemented and is a nebulous situation.

The suggestion that the Federal Radiation Council (FRC), in some form, be revived, also is not without problem. The perceived domination of such a group by an operational agency with its own goals in mind must never be allowed to occur.

As an alternative to the above study recommendation and suggestion, the Conference recommends consideration by Congress of the following:

1) The establishment in the Office of the President of the United States of an overview council with agency representation to include, but not limited to, the following:

(a) The Administration of DHEW
(b) The Administration of EPA
(c) The Commission of NRC
(d) The Administration of DOE
(e) The Administration of DOL
(f) The Administration of DOT

The coordination of this council should be in the Office of Management and Budget (OMB) as the allocation of funds authorized by Congress to accomplish the tasks assigned resides with that office.

This council should be given the legislative authority to review and evaluate the methods, action, or non-actions on Federal guidance implementation and other pertinent matters relating to the full scope of radiation protection. Authorization should also be given to this council to require realignment or programs if an agency is not performing its responsibilities in accord with the respective statutes and the Federal guidance.

Outside technical advisors to this council should be mandatory and should include, but not be limited to, such groups as:

BEST COPY AVAILABLE

(a) the International Committee for Radiation Protection
(b) the National Council on Radiation Protection and Measurement
(c) the National Bureau of Standards
(d) the Conference of Radiation Control Program Directors, Inc.

2) The Federal guidance development responsibility must be more accurately and completely defined to address the totality of the radiation protection concerns. Radiation protection guidance for both ionizing and non-ionizing must be provided for the worker, patient, general public and the environment exposures relative to radiation and radioactive materials. The agency or council assigned this responsibility must not be encumbered with additional responsibility of the development of specific regulatory provisions implementing such Federal guidance or other conflicting assignment of tasks.

The Conference of Radiation Control Program Directors, as a group of state and local government officials who daily address the problems of radiation protection, sees the Federal lack of central focus and coordination seriously affecting their respective programs of protecting the public health, safety and the environment. The Conference is the coordinating and focal point for state and local radiation protection programs alleviating the problem at that level except for Federal intervention. We offer our services in providing assistance and advice individually or as the Conference to the Congress and to the agencies or council, as suggested above.

We concur with the efforts that Congress is expending in this area to provide direction to the radiation protection efforts to the Federal programs. While the Conference would prefer a single agency responsible for radiation protection at the Federal level, the suggestions provided herein should definitely improve the situation. Hopefully, with appropriate Congressional action, this matter will get the attention this matter fully deserves and requires.

If we may be of any further service, please advise.

Sincerely,

Alice T. Dolezal

Ms. Alice T. Dolezal,
Chairwoman

BEST COPY AVAILABLE

Mr. Rogers. Thank you, Ms. Dolezal. Dr. Carter.

Mr. Carter. Thank you.

What are some of the problems that States encounter in dealing with the Federal Government with respect to radiation control?

Ms. Dolezal. There are a number of them, Dr. Carter. As I indicated in one area, the problem is a variety of standards. Sometimes difference in standards, contradictory standards, or at least different enough that making implementation is very difficult.

Another area is providing sufficient funding to continue the tasks that would be necessary to accomplish the objective of the Federal standards.

Mr. Carter. Do most States have radiation control programs concentrated in a single agency?

Ms. Dolezal. Yes, Dr. Carter, most of them do.

Mr. Carter. What is the conference doing to improve quality control in the taking of radiographs?

Ms. Dolezal. There are a number of things. First of all, we have tried to identify the factors which would be necessary to improve the quality control. We are looking at the equipment which would be necessary to measure such things and then working with individual locations, individual facilities.

There are a number of areas, identified by the task force, that we have specifically working on quality control showing that a great deal of work still needs to be done. But a start has been made.

Mr. Carter. What about the problem of retakes? What percentage of films are retaken?

Ms. Dolezal. It is very difficult for us to ascertain that. To the extent that is a part of our inspections, many of us are restricted in that area, which would not include not specifically asking that question.

The area of film development, the area of positive beam limitation, or in some way looking at the machine, we can determine there would be some. We do not have a direct means for finding out specifically the answer to that question.

Mr. Carter. Over the years, though, this has been improved particularly by film development process.

Ms. Dolezal. That is correct.

Mr. Carter. The process has been speeded up and made much easier.

In the State of Minnesota, do you require X-ray technicians to wear film badges or similar apparatus?

Ms. Dolezal. We have a State rule that says if an individual is likely to or may get 25 percent of the maximum limit, then that individual must wear the film badge; that is correct.

Mr. Carter. What is the maximum limit in Minnesota? Is there often a difference between the State standard and Federal standards?

Ms. Dolezal. We are identical with the Federal standard, the five rem per year.

Mr. Carter. Do you think that is a good standard?

Ms. Dolezal. I know there is discussion on the actual setting of that standard. We are looking at that. At this time, the State has adopted the position that that is an adequate standard until we find reason to direct otherwise.

Mr. CARTER. It has been recommended by some that it be reduced tenfold to .5 rems.

Is the Conference concerned about the efficacious use of X-rays?

Ms. DOLEZAL. Yes, Doctor, we are. We have, as I indicated, a task force being set up to look at it. This has been under discussion, and it is an area we are quite concerned about.

Mr. CARTER. It is an area for regulatory and professional action; is that correct?

Ms. DOLEZAL. That is correct.

Mr. CARTER. And you are proceeding with that?

Ms. DOLEZAL. That is correct.

Mr. CARTER. Thank you very kindly.

Mr. ROGERS. Do the State regulatory programs differ greatly? I presume, from your testimony, they do.

Ms. DOLEZAL. Yes, they do.

Mr. ROGERS. Should there be a minimum standard?

Ms. DOLEZAL. Certain areas, I believe, should have a minimum standard. It is difficult to pinpoint specifically, since each State has to go through its own State procedure, including the State legislature, in setting the particular standard or rule that it has.

Mr. ROGERS. Suppose the Federal Government mandated a minimum program?

Ms. DOLEZAL. If the Federal Government mandated it, there would be no choice on it; that is correct.

Mr. ROGERS. What I am saying is, should there be a choice on a minimum standard?

Ms. DOLEZAL. In certain areas, I think there should be.

Mr. ROGERS. In other words, it is all right for some people in one State to have more exposure than people of another State?

Ms. DOLEZAL. No; I don't mean to indicate that. My understanding of your question would extend to certain areas such as procedures, certain types of practices; things of that sort.

May I just inquire about your question? Were you referring just specifically to exposure when you asked the question?

Mr. ROGERS. I presume that would be one item that you would consider. I also presume you would want to have some minimum for inspection to make sure procedures are carried out.

Ms. DOLEZAL. The guide for inspections or the suggested limit of exposure would be very helpful to States. With the actual number of inspections, we get into the problem of sufficient funds for doing that. This has been a factor, a very determining factor, in the number of inspections, the frequency of inspections per State.

Mr. ROGERS. Yes; I am sure I can understand that.

Mr. CARTER. Mr. Chairman, will you yield on that?

Mr. ROGERS. Yes.

Mr. CARTER. Don't you collect those film badges from technicians throughout the State regularly? Or aren't they sent in to you, so that you can determine their exposure?

Ms. DOLEZAL. We look at them; we examine them during our surveys. We do not actually collect them ourselves.

Mr. CARTER. Who collects them?

Ms. DOLEZAL. The facility collects the film badge.

Mr. CARTER. What facility?

Ms. DOLEZAL. The hospital or the office; whichever facility.

Mr. **Carter**. It is done differently in some States. I know in our area, we do have those monitors. They are collected, as I understand it, by State agencies and are monitored. So if anyone gets close to the 5 rem rate, they are not exposed for the balance of the year.

Thank you, Mr. Chairman.

Mr. **Rogers**. I notice you said "It should be clear from the previous discussion that unnecessary exposure to X-ray is perceived to be a problem by the Conference." Is there doubt about that?

Ms. **Dolezal**. It is difficult to say what precisely is unnecessary until some specific amount is put as the correct amount or overexposure.

Mr. **Rogers**. Do I understand it, then, it is not generally accepted that unnecessary exposure is bad?

Ms. **Dolezal**. That is generally accepted. The part that is difficult is where do you start; what is needed exposure for the radiograph? Then anything above that becomes unnecessary. That needed exposure level is the difficult part to determine; exactly how much. And this is part of what we hope to work with in the quality assurance; to get the needed exposure amount determined.

Mr. **Rogers**. You are saying right now we simply don't know how much exposure we should use, say, to get a particular picture and whether it has the validity for the cause for which it was taken.

Mr. **Carter**. Mr. Chairman, if you would permit, I believe we know the amount of exposure that it takes to get a good film. We know the number of amps. But what you want to arrive at is a safe level, a safe standard, as I see it.

So far as I know, we have a standard of 5 rems per year for occupational exposure, and in some cases it can be exceeded and can go up to 12 rems/year.

Ms. **Dolezal**. For the occupational exposure. For the patient exposure, to get back to your question, Congressman, there are some differences among the practitioners as to what the best radiograph is and, therefore, differences in the amount of radiation necessary to achieve that.

Mr. **Rogers**. Should the minimum that is accepted and used be the rule or should it be the maximum?

Ms. **Dolezal**. Ordinarily the principle would be the minimum amount necessary to achieve a diagnostically good radiograph.

Mr. **Rogers**. Do you have the authority in your State, if you find a defective machine, to put it out of service until it is corrected?

Ms. **Dolezal**. We have the authority to have the machine closed down or made inoperable if we determine a serious health hazard.

Mr. **Rogers**. Not a malfunctioning of the device?

Ms. **Dolezal**. If the malfunction, in turn, causes a serious health hazard, then the answer is yes.

Mr. **Rogers**. How do you determine what is a serious health hazard? If the machine just isn't working, you don't close it down?

Ms. **Dolezal**. That would depend upon which particular type of malfunction there is. If it is a case of the light on a particular dial does not work, the dial is actually otherwise functioning, that would be the kind of malfunction which would not require any immediate cessation, but immediate action to make sure that it is corrected.

On the other hand, if there is a type of malfunction in which the patient receives a large amount of radiation, that is a health hazard and that is the type of malfunction which would, indeed, call——

Mr. **Rogers.** So your State has that authority?

Ms. **Dolezal.** Yes.

Mr. **Rogers.** Have you exercised it?

Ms. **Dolezal.** Yes; we have.

Mr. **Rogers.** How often?

Ms. **Dolezal.** Infrequently. I would say a couple times annually, possibly.

Mr. **Rogers.** How do you make sure it is corrected?

Ms. **Dolezal.** Inspection immediately.

Mr. **Rogers.** Before it can be operated again?

Ms. **Dolezal.** Right.

Mr. **Rogers.** And you would test it?

Ms. **Dolezal.** That is correct.

Mr. **Rogers.** People from your office?

Ms. **Dolezal.** That is correct.

Mr. **Rogers.** What type of malfunctions?

Ms. **Dolezal.** The malfunctions really can vary with the variety of systems that there are. The malfunction, as I picked out one particular one earlier of a dial that might be malfunctioning, that could be the amperage dial or the kVp; that type of malfunction. It could be there is a malfunction in the collimator or some particular part on the collimator which would restrict or not permit collimation to occur, which, of course, would be a very serious one.

There could be malfunction in being able to move the tube properly. Any of those could be malfunctions.

Mr. **Rogers.** Are these set forth in regulations that you have?

Ms. **Dolezal.** Yes, they are.

Mr. **Rogers.** Would you let the committee have a copy of those for the record?

Ms. **Dolezal.** Certainly.

[Testimony resumes on p. 619.]

[The following material was received for the record:]

MINNESOTA STATE REGULATIONS

Rules and Regulations of

MINNESOTA DEPARTMENT OF HEALTH

Relating to

Ionizing Radiation

1971 EDITION

Filed with the Secretary of State
and Commissioner of Administration Sept., 1971.

Cite the regulations as:
(for example)
MHD 181

Distributed by
DOCUMENTS SECTION, DEPARTMENT OF ADMINISTRATION
Room 140 Centennial Building, St. Paul, Minnesota 55155

CHAPTER TWENTY-ONE

TABLE OF CONTENTS

Regulation

- **MHD 181 General Provisions**
  - **(a) Declaration of Purpose and Scope**
  - **(b) Definitions**
  - **(c) Precautionary Procedures**
    - **(1) Radiation Symbol and Labeling**
    - **(2) Personnel Monitoring**
  - **(d) Registration**
    - **(1) Registration Requirements**
    - **(2) Renewal of Registration**
    - **(3) Records, Inspections, and Tests**
    - **(4) Exemptions**
  - **(e) Vendor Responsibility**
  - **(f) Transportation**
  - **(g) Notification of Incidents and Lost Sources**
  - **(h) Restrictions**
    - **(1) Prohibitions**
    - **(2) Violations**
  - **(i) Special Provisions**
    - **(1) Safety and Precaution**
    - **(2) Shielding**

- **MHD 182 X-Ray Uses**
  - **(a) Healing Arts**
    - **(1) Fluoroscopic**
    - **(2) Radiographic Installations Other than Dental, Veterinary Medicine, and Industrial**
    - **(3) Special Requirements for Mobile Diagnostic Radiographic Equipment Other than Dental, Veterinary Medicine, and Industrial**
    - **(4) Special Requirements for Chest Photofluorographic Installations**
    - **(5) Dental Radiographic Installations**
    - **(6) Therapeutic X-Ray Installations**

Regulation

(7) Special Requirements for X-Ray Therapy Equipment Operated at Potentials of 60 Kilovolts and Below

(8) Veterinary Medicine Radiographic Installations

(b) Industrial

MHD 183 Radium Uses

(a) Healing Arts

(b) Industrial Radium Installation

(c) Waste Disposal of Radium Sources

MHD 184 Special Uses of Electric Equipment

(a) Accelerators, X-Ray Diffraction Units and Electron Microscopes

(b) Television Receivers

(c) Research and Teaching Institutions

MHD 185 Nuclear Facilities

Minnesota State Board of Health

REGULATIONS ON IONIZING RADIATION

CHAPTER TWELVE

MHD 181 General Provisions

(a) Declaration of Purpose and Scope

Whereas, ionizing radiation can be instrumental in the improvement of health, welfare, and productivity of the public if properly utilized, and may impair the health of the people and the industrial and agricultural potentials of the State if improperly utilized, and the Board has the statutory authority and duty to adopt, alter, and enforce regulations for the preservation of the public health and thereby to control sources of ionizing radiation and the handling, storage, transportation, use, and disposal of radioactive isotopes and fissionable materials within this State, and to observe their effect upon human health, it is hereby declared to be the purpose of the Board in these regulations to secure information concerning the nature and extent of the employment of radiation-emitting equipment and radioactive materials within this State, and to control or prevent dangers to health from ionizing radiation without limiting or interfering with the constructive uses of radiation consistent with a policy of reducing radiation exposure to persons and the general public by all practical means. The scope of these regulations does not include, except for the provision of registration, those sources of ionizing radiation known as byproduct materials, source materials, or special nuclear material.

(b) Definitions

Appropriate limit or appropriate limits—The maximum permissible dose or doses of radiation that may be administered to the whole body or a given part of a human being. See "maximum permissible concentrations," "maximum permissible doses," and "maximum permissible neutron radiation."

Attenuation—The reduction of exposure rate upon passage of radiation through matter.

Board—The Minnesota State Board of Health.

Collimation—The restriction of the useful beam to an appropriate area.

Commissioner—The Commissioner of the Minnesota Department of Health.

Controlled area—A defined area in which the exposure of persons to radiation is under the supervision of a Radiation Protection Supervisor. (This implies that a controlled area is one that requires control of access, occupancy, and working conditions for radiation protection purposes.)

Curie (Ci)—The special unit of activity equal to a disintegration rate of 37 billion disintegrations per second. One millicurie (mCi) equals 0.001 curie; one microcurie (uCi) equals 0.000001 curie.

Dead-man switch—A switch so constructed that a circuit-closing contact can be maintained only by continuous pressure on the switch.

Diagnostic-type protective tube housing—An x-ray tube housing so constructed that the leakage radiation measured at a distance of 1 meter from the source cannot exceed 100 milliroentgens in 1 hour when the tube is operated at its maximum continuous rated current for the maximum rated tube potential.

Dose equivalent (DE)—A quantity used for radiation protection purposes that expresses on a common scale for all radiations the irradiation incurred by exposed persons. It is defined as the product of the absorbed dose in rads and certain modifying factors. The unit of dose equivalent is the rem. (The modifying factors are:

1 for gamma and x rays and beta particles
10 for alpha particles and for neutrons
10 for protons with energies up to 10 million electron volts
20 for heavy ions

For x and gamma rays, the dose in rems may be assumed to be numerically equivalent to the exposure in roentgens and the absorbed dose in rads.)

Filter-filtration—Material in the useful beam which absorbs preferentially the less penetrating radiation.

Healing arts—Health professions for diagnostic and/or healing treatment of human and animal maladies including but not limited to the following which are duly licensed by the State of Minnesota for the lawful practice of: medicine and its associated specialties, dentistry, veterinary medicine, osteopathy, chiropractic, and podiatry.

Half-value layer (HVL)—Thickness of a specified substance which, when introduced into the path of a given beam of radiation, reduces the exposure rate by one half.

High radiation area—Any area, accessible to individuals, in which there exists radiation at such levels that a major portion of the body could receive in any 1 hour a dose in excess of 100 millirem.

Industrial radiographer—Any individual who performs or who, in attendance at the site where sources of radiation are being used, personally supervises industrial radiographic operations and who is responsible to the registrant for assuring compliance with the requirements of these regulations.

Industrial radiography—The examination of the macroscopic structure of materials by nondestructive methods utilizing sources of radiation.

Inherent filter—The filter permanently in the useful beam; it includes the window of the x-ray tube and any permanent tube or source enclosure.

Interlock—A device which automatically causes a reduction of the exposure rate upon entry by personnel into a high radiation area. Alternatively, an interlock may prevent entry into a high radiation area.

Ionizing radiation—See radiation.

Iso-line—A line, usually irregular, along which the exposure rates are the same at any point.

Kilovolt peak (kVp)—The crest value in kilovolts of the potential difference of a pulsating potential generator. When only one half of the wave is used, the value refers to the useful half of the cycle.

Lead equivalence–The thickness of lead affording the same attenuation, under specified conditions, as the material in question.

Leakage radiation–See radiation.

Maximum permissible concentrations (MPC)–Those amounts listed as maximum permissible concentrations in Handbook 69, "Maximum Permissible Body Burdens and Maximum Permissible Concentrations of Radionuclides in Air and in Water for Occupational Exposure," U. S. Department of Commerce, National Bureau of Standards, June 5, 1959.

Maximum permissible dose or dose equivalent (MPD)–For radiation protection purposes, the maximum dose equivalents that persons shall be allowed to receive in a stated period of time (see Table 1 in the Appendix). This excludes patients receiving radiation for diagnostic or therapeutic purposes under supervision of licensed practitioners of the healing arts.

Maximum permissible neutron radiation–The amount of neutron radiation in rems that is equivalent to the maximum permissible dose. Neutron flux dose equivalents are given in Table 2 of the Appendix.

One general site–The building or adjacent buildings at the same address in which the sources of ionizing radiation for the registrant are located.

Person–Any individual, corporation, partnership, firm, association, trust, estate, public or private institution, group, agency, political subdivision of this State, and any legal successor, representative, agent or agency of the foregoing, but not federal government agencies.

Personnel monitor–An appropriately sensitive device used to estimate the radiation exposure of an individual, (e.g., film badges, pocket chambers, pocket dosimeters, film rings, thermo-luminescent dosimeters, and other devices having the same purpose).

Picocurie–A micromicrocurie or that quantity of radioactive material which decays at the rate of 2.2 disintegrations per minute.

Primary beam–See radiation: useful beam.

Primary protective barrier–See protective barrier.

Protective apron–Apron made of radiation absorbing materials, used to reduce radiation exposure.

Protective barrier–A barrier of radiation absorbing material(s) used to reduce radiation exposure.

Primary protective barrier–Barrier sufficient to attenuate the useful beam to the required degree.

Screening–The testing with x-ray machines of human beings or human population groups for the detection or evaluation of health conditions when such x-ray tests are not specifically and individually ordered by a licensed healing arts practitioner, legally authorized to order such x-ray tests, 1) for the purpose of diagnosis or treatment or 2) as part of a physical examination conducted by a licensed practitioner. Screening does not include research protocols utilizing x-ray procedures when such protocols are part of research projects 1) sponsored or financed by agencies of the federal government, 2) conducted by educational institutions training practitioners of the healing arts or, 3) conducted in hospitals, when such research is authorized by or under control of the governing body of that hospital.

Secondary protective barrier–Barrier sufficient to attenuate stray radiation to the required degree.

Protective glove–Glove made of radiation absorbing materials used to reduce radiation exposure.

Rad–A special unit of absorbed dose equal to 100 ergs per gram. One millirad (mrad) equals 0.001 rad.

Radiation–(Ionizing) Any electromagnetic or particulate radiation capable of producing ions directly or indirectly, by interaction with matter. (This includes gamma rays and x rays, alpha and beta particles, high-speed electrons, neutrons, protons, and other nuclear particles, but does not include sound or radio waves, or visible, infrared or ultraviolet light.)

Leakage radiation–All radiation coming from within the source or tube housing except the useful beam. (Note: Leakage radiation includes the portion of the direct radiation not absorbed by the protective source or tube housing as well as the scattered radiation produced within the housing.)

Scattered radiation–Radiation that, during passage through matter, has been deviated in direction. (It may have been modified also by a decrease in energy.)

Secondary radiation–Radiation emitted by an irradiated material such as bone or tissue and all inanimate objects.

Stray radiation–The sum of leakage and scattered radiation.

Useful beam–Radiation which passes through the window, aperture, cone or other collimating device of the source housing. Sometimes called "primary beam."

Radiation hazard–A condition under which persons might receive radiation in excess of the maximum permissible dose.

Radiation machine–Any device capable of producing radiation except devices which produce radiation only from radioactive material.

Radiation protection–The use of shielding, protective clothing, protective equipment, and other means to eliminate or reduce exposure to ionizing radiation.

Radiation protection survey–See survey.

Radiation Safety–A condition assumed to exist when following a policy of minimization the doses of radiation are eliminated or reduced to the lowest practicable amount and are less than those shown under the definitions of maximum permissible concentrations, maximum permissible doses, and maximum permissible neutron radiation.

Radioactive material–Any solid, liquid, or gaseous substance which emits radiation spontaneously.

Radiographic exposure device–Any device containing a sealed source, fastened or contained therein in which the sealed source or shielding thereof may be moved, or otherwise changed, from a shielded to an unshielded position for purposes of making a radiographic exposure.

Registrant—A person having possession of any source of ionizing radiation except those specifically exempted under MHD 181 (d) (1) or MHD 181 (d) (4), who has complied with MHD 181 (d) (1).

Rem—The unit of dose equivalent. One millirem (mrem) equals 0.001 rem.

Restricted area—Any area to which access or egress may be limited by the registrant for purposes of protection of individuals from exposure to radiation and radioactive materials.

Roentgen (R)—A special unit of exposure equal to 2.58 x 10^{-4} coulomb per kilogram of air. One milliroentgen (mR) equals 0.001 roentgen.

Scattered radiation—See radiation.

Secondary protective barrier—See protective barrier.

Secondary radiation—See radiation.

Source—A discrete amount of radioactive material or the target (focal spot) of the x-ray tube.

Storage container—A device in which sources are transported or stored.

Stray radiation—See radiation.

Survey—An evaluation of the adequacy of radiation protection and assessment of the situation incident to the production, use, release, disposal, or presence of sources of ionizing radiation under a specific set of conditions. When appropriate, such evaluation includes a physical survey of the location of materials and equipment, and measurements of levels of radiation or concentrations of radioactive material present in and around the installation.

Television receiver—An electronic product designed to receive and display a television picture through broadcast, cable, or closed-circuit television.

Therapeutic-type protective tube housing—

(1) For x-ray therapy equipment not capable of operating at 500 kilovolt peak (kVp) or above, the following definition applies: An x-ray tube housing so constructed that the leakage radiation at a distance of 1 meter from the source does not exceed 1 roentgen in an hour when the tube is operated at its maximum rated continuous current for the maximum rated tube potential.

(2) For x-ray therapy equipment capable of operation at 500 kilovolt peak (kVp) or above, the following definition applies: An x-ray tube housing so constructed that leakage radiation at a distance of 1 meter from the source does not exceed either 1 roentgen in an hour or 0.1 percent of the useful beam dose rate at 1 meter from the source, whichever is greater, when the machine is operated at its maximum rated continuous current for the maximum rated accelerating potential.

(3) In either case, small areas of reduced protection are acceptable provided the average reading over any 100 square centimeters area at 1 meter distance from the source does not exceed the values given above.

Unit of exposure—The roentgen.

Unit of radioactivity—The curie.

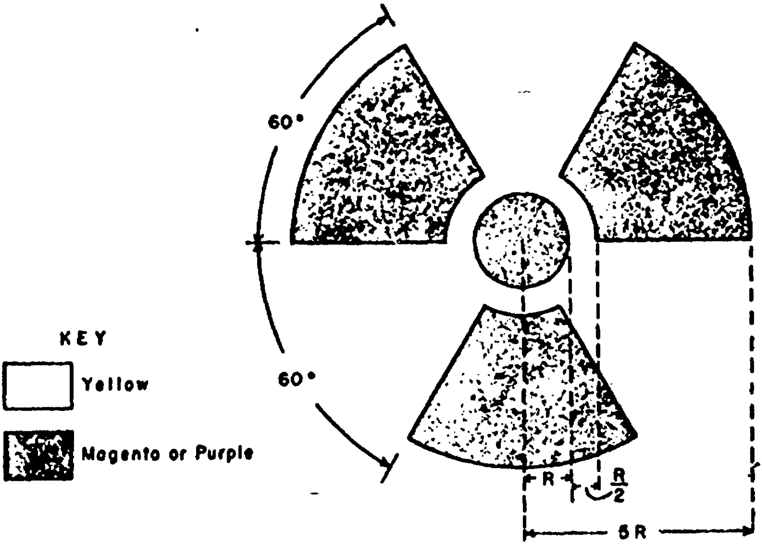
Units of radiation dose—The rad (unit of absorbed dose) and the rem (radiation to body tissues in terms of its estimated biological effect relative to an exposure of 1 roentgen of x ray).

Useful beam—See radiation.

(c) Precautionary Procedures

(1) Radiation Symbol and Labeling

(aa) Each radiation sign or label shall bear the standard symbol specified in these regulations and the specified printed warning in capital block letters. The warning CAUTION RADIATION AREA or DANGER RADIATION AREA shall appear on signs in an area in which a radiation hazard may exist. The warning CAUTION, RADIOACTIVE MATERIAL(S) or DANGER, RADIOACTIVE MATERIAL(S) shall appear on containers containing radioactive materials greater than the applicable quantities listed in Tables 3 and 4 in the Appendix. The standard symbol for designating any radiation hazard shall be a circle with three propeller-like blades arranged around it as illustrated:



The boundaries of the three blades of the propeller-like symbol shall be confined within a 60° sector of the circle delineated by their outer edges, and said blades shall be symmetrically distributed 60° apart. The radius (R) of the central circle of the symbol shall be the standard for its other dimensions as follows: Overall radius of symbol = 5R, shortest distance from circumference of central circle to inner edge of nearest blade = R/2. The standard color specifications shall be a background of yellow with lettering and distinctive symbol in magenta or purple. The symbol and lettering shall be as large as practical, consistent with the size of the equipment or material upon which they appear.

(bb) The use of the specified radiation symbol for any other purpose than designating or referring to an area of detectable radiation is expressly prohibited.

(cc) All containers of radioactive material for storage and disposal, storage areas, work areas, and other normally occupied areas where a radiation hazard may exist shall be conspicuously posted with radiation warning labels.

(dd) Conspicuous radiation warning labels shall be posted in areas which are not readily accessible and may be only occasionally occupied but in which a radiation hazard may exist.

(ee) Readily accessible areas in which a radiation hazard may exist shall be suitably delineated and conspicuously posted with radiation warning labels. This applies even if the area is not normally occupied.

(ff) All radiation-hazard labels posted when a radiation hazard existed shall be removed when the hazard is no longer present.

(2) Personnel Monitoring

(aa) Each registrant shall supply appropriate personnel monitoring equipment to, and shall require the use of, such equipment by:

(i) Each individual, except a patient, who enters a restricted area under such circumstances that he or she receives, or is likely to receive, a dose in excess of one quarter of the maximum permissible dose as defined in these regulations.

(ii) Each individual who enters a high radiation area.

(bb) Records of exposures shall be maintained permanently by the registrant.

(d) Registration

(1) Registration Requirements. The owner or person having possession of any source of ionizing radiation except those specifically exempted under this regulation or under MHD 131 (d) (4) or in the case of nuclear facilities which are registered in accordance with special procedures required by MHD 185, shall:

(aa) Register such sources with the Board within 30 days of its acquisition upon forms prescribed and provided for that purpose.

(bb) Designate an individual who will be responsible for radiation protection from the source. Such individual, the radiation protection officer, shall:

(i) Be qualified by training and experience concerning all hazards and precautions involved in operating or in using the source for which he is responsible;

(ii) establish a detailed program of radiation safety for effective compliance with the applicable requirements of these regulations;

(iii) give instructions concerning hazards and safety practices to individuals under his supervision who may be exposed to radiation from the source; and

(iv) make surveys and carry out other procedures as required by these regulations.

When, in the opinion of the Board, the individual designated to be responsible for radiation safety does not have qualifications sufficient to insure safe operating or using of the source, the Board may require the registrant to designate another individual who meets the requirements of MHD 181 (d) (1) (bb) above.

(cc) Every hospital in which radioisotopes are used shall have a committee which coordinates the use of radioisotopes within the hospital and assures the radiation safety of the patients and personnel involved during the use of these isotopes.

(dd) The registrant shall notify the Board within 30 days of any change in the ownership or disposition of registered sources.

(ee) No person in any advertisement shall refer to the fact that a source is registered with the Board, and no person shall state or imply that any activity under such registration has been approved by the Board.

(ff) The registrant shall be subject to all applicable requirements of these regulations.

(gg) The registration requirements shall not apply to facilities subject to MHD 185, nor to sources or conditions exempted under MHD 181 (d) (4), nor to by-product materials, source materials, or special nuclear materials licensed by the U. S. Atomic Energy Commission not in excess of the kind and quantity specified in Tables 3 and 4 of the Appendix.

(2) Renewal of Registration. Each registration pursuant to these regulations shall be renewed biennially during the month of January of odd-numbered years so long as the activity requiring registration continues. If there has been no substantial change in the matters described in the last prior registration or renewal, the renewal of the registration shall so state. If there has been any accession of additional radiation sources or other substantial change in the matters described in the preceding registration or renewal, the renewal shall state the accession or other change and give the information relating to such accession or other change that would be required upon original registration.

(3) Registration Fees.

(aa) The initial or renewal biennial registration of every source of ionizing radiation required to be registered by Minn. Rule MHD 181 (d) shall be accompanied by a fee as prescribed herein. The fee shall be based upon the number of x-ray tubes and facilities using radium registered by each person, company, hospital, group, practice, or other organization or association at one general site as follows:

(i) First tube, $30.00;

(ii) Each additional tube not to exceed 15 additional tubes, $10.00 per tube;

(iii) Each facility using radium, $100.00.

(bb) Applications for initial or renewal registrations submitted to the Board after the time specified by these rules shall be accompanied by a penalty fee, in addition to the fee prescribed in Minn. Rule MHD 181 (d) (3) (aa), as follows:

(i) For applications submitted up to 30 days after the required initial or renewal date, $5.00;

(ii) For applications submitted between 31 and 60 days after the required initial or renewal date, $10.00;

(iii) For applications submitted 60 days or more after the required initial or renewal date, $15.00.

(cc) The initial registration fee for any source of ionizing radiation required to be registered during the last three months of a biennial registration period shall be $5.00 per x-ray tube up to a maximum of 16 tubes and $20.00 for each facility using radium. The penalty fees as specified in Minn. Rule MHD 181 (d) (3) (bb) shall apply to this section. This provision shall not apply to any application for registration which should have been submitted to the Board in a timely manner prior to the last three months of a registration period.

(4) **Records, Inspections, and Tests.**

(aa) Each registrant shall keep records showing the receipt, transfer, and disposal of all sources of radiation subject to these and all other state and federal regulations.

(bb) Each owner, renter, or other person in possession of a source of radiation subject to registration or expected under MHD 181 (d) (1) or MHD 181 (d) (4) shall afford agents of the Board, at all reasonable times, opportunity to inspect sources of radiation and the premises and facilities wherein such sources of radiation are used or stored, and shall make available to the agent, upon reasonable notice, records maintained pursuant to these regulations.

(cc) Each owner, renter, or other person in possession of a source of radiation shall perform or cause to be performed such reasonable procedures as are necessary to assure radiation safety including, but not limited to, tests of:

(i) Sources of radiation;

(ii) facilities wherein sources of radiation are used or stored; and

(iii) radiation detectors, monitoring instruments, and other equipment and devices used in connection with utilization or storage of sources of radiation.

Results of such tests shall be available for submission to the Board when requested.

(5) **Exemptions.** These regulations shall not apply to the following sources or conditions:

(aa) Natural radioactive materials of an equivalent specific radioactivity not exceeding that of natural potassium;

(bb) timepieces, instruments, or devices containing self-luminous elements, except during manufacture or repair of the self-luminous elements themselves;

(cc) electrical equipment that is not intended primarily to produce radiation and that, by nature of design, does not produce radiation at the point of nearest approach at a weekly rate higher than one tenth (1/10) of the appropriate limit for any critical organ exposed. The production testing or production servicing of such equipment shall not be exempt;

(dd) a radiation machine not being used in a manner such that it produces radiation;

(ee) domestic television receivers, provided the dose rate at 5 cm from any outer surface of 10 cm^2 is less than 0.5 mrem per hour;

(ff) any radioactive material being transported in conformity with regulations adopted by the U. S. Department of Transportation and other agencies of the United States having jurisdiction;

(gg) any quantities of thorium contained in

(i) incandescent gas mantles

(ii) vacuum tubes

(iii) welding rods

(iv) electric lamps for illuminating purposes provided that each lamp does not contain more than 50 milligrams of thorium

(v) germicidal lamps, sunlamps, and lamps for outdoor or industrial lighting provided that each lamp does not contain more than 2 grams of thorium; and

(vi) rare earth metals and compounds, mixtures, and products containing not more than 0.25 percent by weight thorium, uranium, or any combination of these.

(hh)radiation sources specifically designated by the Board as exempt by virtue of being known to be without hazard to health.

(e) Vendor Responsibility

(1) No person shall make, sell, lease, transfer, lend, or install x-ray or fluoroscopic equipment or the supplies used in connection with such equipment unless such supplies and equipment, when properly placed in operation and properly used, will meet the requirements of these regulations. This includes, but is not restricted to, responsibility for the delivery of cones or collimators, filters, adequate timers, and fluoroscopic shutters (where applicable).

(2) Persons selling, leasing, or transferring registerable sources of radiation shall notify the Board in writing within 30 days of such sale, lease, or transfer, and shall supply the name and address of the purchaser and such pertinent information as is requested by the Board.

(f) Transportation

(1) The provisions of this section apply to the transportation of radioactive materials or the delivery of radioactive material to a carrier for transportation, not subject to the rules and regulations of the U. S. Department of Transportation and other agencies of the United States having jurisdiction.

(2) No person shall transport any radioactive material outside the confines of the facility or other authorized location of use, or deliver any radioactive material to a carrier for transportation, unless the person complies with all requirements, appropriate to the mode of transportation, relating to the packaging of the radioactive material and to the marking and labeling of the package and transporting vehicle, of the rules and regulations, published by the U. S. Department of Transportation (46 C.F.R., Part 146, 49 C.F.R., Parts 173-179, and 14 C.F.R., Part 103) to the same extent as if the transportation were subject to the rules and regulations of that agency.

(g) Notification of Incidents and Lost Sources

(1) Immediate Notification. The owner, operator, radiation safety officer, or the person in charge of the radiation source shall immediately notify the Board by telephone or telegraph of any incident involving registered sources of ionizing radiation which may have caused, or threatens to cause:

(aa) A dose equivalent to the whole body of any individual of 25 rems or more of radiation;

(bb) a dose equivalent to the skin of the whole body of any individual of 150 rems or more of radiation; or

(cc) a dose equivalent to the feet, ankles, hands, or forearms of any individual of 375 rems or more of radiation.

(2) Twenty-four Hour Notification. The owner, operator, radiation safety officer, or the person in charge of the radiation source shall within 24 hours notify the Board by telephone or telegraph of any incident involving registered sources of ionizing radiation which may have caused, or threatens to cause:

(aa) A dose equivalent to the whole body of any individual of 5 rems or more of radiation;

(bb) a dose equivalent to the skin of the whole body of any individual of 30 rems or more of radiation; or

(cc) a dose equivalent to the feet, ankles, hands, or forearms of any individual of 75 rems or more of radiation.

(3) When a theft or loss of a radiation source occurs, the owner, operator, radiation safety officer, or the person in charge shall notify the Board by telephone immediately upon discovery of the situation and shall report all known facts and circumstances relating to the occurrence in writing within 7 days thereafter. The owner shall notify the Board of actions taken to recover the stolen or lost source and shall report any substantive additional information on the loss or theft which becomes available to the registrant within 30 days after he learns of such information.

(h) Restrictions

(1) Prohibitions

(aa) Because of the public health hazard involved in the indiscriminate use of radiation, it is hereby prohibited for any person to operate or maintain within the State any shoe-fitting fluoroscopic device.

(bb) Radiation shall not be applied to a person for the purpose of instruction or training.

(cc) Only those individuals who are licensed practitioners of the healing arts, or individuals that are qualified by training and experience and are under the direct supervision of a licensed practitioner of the healing arts, may intentionally apply radiation to a person.

(dd) The use of x-ray machines for the purpose of screening is prohibited without prior written approval of the Commissioner.

(2) Commissioner approval of screening. Any person desiring Commissioner approval for screening purposes as specified in MHD 181 (h) (1) (dd) shall submit an application to the Commissioner requesting his permission to perform screening. The burden of justifying the requested screening rests on the applicant. Approval will be granted if the Commissioner is satisfied that:

(aa) The proposed screening is a justified public health measure;

(bb) The benefit derived from the proposed screening will outweigh the detriment of x-ray exposure; and

(cc) The x-ray screening will be conducted properly, safely, and legally, i.e., in accordance with all applicable statutes and rules of the State of Minnesota or federal government.

(3) Content of application for approval of screening. The application for approval of a screening program must contain the following information and data:

(aa) Name and Minnesota business address.

(i) If the applicant is a corporation or other business or non-business association, the name of the person representing the association shall be given.

(ii) If the applicant's principal location or home office is not in Minnesota, the principal location or home office address shall be given as well as the name of the person who may be contacted by the Commissioner with respect to the application.

(iii) If the applicant is a foreign corporation subject to the provisions of Minnesota Statute Chapter 303 it shall submit a certified copy of its Certificate of Authority issued by the Minnesota Secretary of State. The certification shall be dated no more than one month prior to the date of submission of the application to the Commissioner.

(bb) When and where the proposed screening is to be performed.

(cc) Description of the specific screening proposed.

(dd) Description of the age distribution of the population to be screened.

(ee) The amount of x-ray exposure to which individuals will be subjected by the proposed screening.

(i) Applications for screening for pulmonary (lung) conditions shall not be approved if the incident (skin entrance) x-ray exposure will exceed 50 milliroentgens per radiograph for the posterior-anterior (PA) view. Using normally accepted exposure techniques, a Victoreen R-chamber placed at a distance of 11 inches from the center of the film with a scatter phantom (Alderson "Rando" phantom or equivalent) positioned in front of the center of the film, or an equivalent method, shall be the method used for measuring the incident (skin entrance) exposure.

(ii) Commonly accepted state-of-the-art techniques and equipment shall be the methods used for measuring x-ray exposure from other types of screening. A written description of the specific method used shall be submitted to the Commissioner. The amount of x-ray exposure shall be specified as skin entrance or film exposure and shall not exceed amounts normally given during such projections based on the studies "Population Exposure to X-Rays U. S. 1970" (DHEW Publication (FDA) 73-8047, November 1973)[1] and "National Evaluation of X-Ray Trends: Tabulation of Data for 'All States' for Period January 1, 1974 to December 31, 1974".[2]

(ff) Why the screening is being planned. A detailed statement shall specify the compelling health reasons, health benefits, or health emergency which justifies the radiation exposure to which individuals will be subjected by the proposed screening.

---

[1] The estimated mean exposure per film by type of radiographic examination specified in this publication is reproduced in Appendix A.

[2] The weighted mean indexes by type of exam/projection specified in this publication are reproduced in Appendix B.

(gg) Who will interpret the x-ray film and to whom will the results, interpretation, or findings be sent.

(hh)Where the x-ray film will be filed.

(ii) Who will have access to the x-ray film.

(jj) If the persons screened will not be given the x-ray film or will not be personally informed by the applicant of the results, interpretation or findings.

(i) How will this information be communicated to those individuals who have been screened.

(ii) What arrangements will be made to assure that those persons who have been screened will be informed as to the need for further medical and health care evalution or treatment.

(kk)Why alternate screening methods, not requiring use of x-ray machines, are not acceptable.

(ll) Who will conduct the screening (operators) and their qualifications, with complete information pertaining to the operators including their formal training and specifically describing any licenses, registration or other authority held from Minnesota or other state or federal agencies or professional associations.

(mm) Who will supervise the operators conducting the screening, with complete information pertaining to the supervisor's qualifications and specifically describing any licenses, registration or other authority held from Minnesota or other state or federal agencies or professional associations. The method of supervision shall be specified.

(nn)What equipment will be used in connection with the screening, and whether it complies with Minnesota law and regulations and whether such equipment has been inspected, licensed or approved in any other way by a Minnesota agency, or by any other state or federal agency.

(oo)Any other information requested by the Commissioner which he deems necessary to enable him to determine whether or not the proposed x-ray exposure the subjects of the screening will receive is a justified public health measure, the benefit of which outweighs the potential detriment of x-ray exposure. The Commissioner may request the submission of additional information and data subsequent to the submission of the original application. The Commissioner may deny approval of any request to perform screening as specified in MHD 181 (h) (1) (dd) if the applicant fails to or refuses to submit all requested data.

(4) Approval of changes in screening program. It is the responsibility of the applicant to inform the Commissioner of any changes in its screening program from that which is described in the application and receive Commissioner approval of such changes prior to commencement of the screening program.

(5) Violations.

(aa) General.[3] If in the opinion of the Commissioner, it is necessary to do so to protect persons from hazards of radiation, an injunction or other court order may be obtained prohibiting any violation of any provision of any regulation or order issued thereunder. Any person who willfully violates any provision of any regulation or order issued thereunder may be guilty of a crime, and, upon conviction, may be punished by fine or imprisonment or both, as provided by law.

---

[3] This subsection (i.e., MHD 181 H.5.a.) already exists in the rules and is not being amended except by being designated as subparagraph "a. General".

(bb)Commissioner Approved Screening.

(i) The Commissioner or his representative may inspect the screening program while in progress to assure that it is being carried out as described in the application and in compliance with Minnesota Rules MHD 181-186 relating to ionizing radiation.

(ii) Approval may be withdrawn immediately if after an inspection the Commissioner finds the existence of conditions which would result in serious overexposure. All screening procedures shall be terminated immediately upon receipt of the written notice of existence of such over-exposure. The applicant may request a contested case hearing within five days after receipt of the notice, provided, however, the request for hearing does not stay the Commissioner's order of immediate cessation of the screening program. The hearing shall be scheduled within ten days of receipt of the request for the hearing.

(iii) Approval may be withdrawn if after an inspection the Commissioner finds discrepancies between the screening program as implemented and as described in the application or for violation of Minnesota Rules MHD 181-186 relating to ionizing radiation. A hearing shall be held if requested by the applicant within three days after the receipt of the notice of withdrawal of approval. The hearing may be held upon granting the applicant three days notice. If a hearing is requested, withdrawal of approval shall not take effect until a final order is issued by the Commissioner.

(i) Special Provisions

(1) Safety and Precaution

(aa) The registrant shall assure himself that each individual operating x-ray equipment under his control is thoroughly conversant with the recommendations of the National Council on Radiation Protection and Measurements pertaining to x rays, currently found in NCRP Report Number 33, "Medical X-Ray and Gamma-Ray Protection for Energies up to 10 MeV," issued February 1, 1968, NCRP Report No. 35, "Dental X-Ray Protection," issued March 9, 1970, NCRP Report No. 36, "Radiation Protection in Veterinary Medicine," issued August 15, 1970, and where applicable National Bureau of Standards Handbook 93, "Safety Standard for Non-Medical X-Ray and Sealed Gamma-Ray Sources," issued January 3, 1964.

(bb)The registrant shall provide safety rules to each individual operating x-ray equipment under his control, including any restrictions of the operating technique required for the safe operation of the particular x-ray apparatus, and shall require that the operator demonstrate familiarity with these rules.

(cc) The amount of ionizing radiation that may be applied to a person for diagnostic purposes shall be the minimum required to obtain the clinical information desired.

(dd)The darkroom for film development shall be light-tight.

(2) Shielding

(aa) Each installation where radiation is used shall be provided with such primary barriers and/or secondary barriers as are necessary to assure radiation safety. Each installation shall comply with the special shielding requirements applicable to the type of installation under consideration as specified in subsequent parts of these regulations. Primary and/or secondary barrier requirements shall be deemed to be met if the thicknesses of such barriers are equivalent to those as computed in accordance with Appendix C, NCRP Report No. 34, "Medical X-Ray and Gamma-Ray Protection for Energies Up to 10 MeV," National Council on Radiation Protection and Measurement, March 2, 1970, and where applicable, National Bureau of Standards Handbook 93, "Safety Standard for Non-Medical X-Ray and Sealed Gamma-Ray Sources," issued January 3, 1964.

(bb)Lead barriers shall be mounted in such a manner that they will not sag or cold-flow because of their own weight and shall be protected against mechanical damage.

(cc) Joints between different kinds of protective materials shall be so designed that the overall protection of the barrier is not impaired.

(dd)Holes in protective barriers shall be covered so that the overall attenuation is not impaired.

(ee) Windows, window frames, doors, and door frames shall have the same lead equivalent as that required of the adjacent wall.

Appendix A
Population Exposure to X-Rays U.S. 1970
Estimated mean exposure per film by type of radiographic examination

Type of Examination	Milliroentgens (at skin entrance)
Head and Neck	300
skull	330
cervical spine	240
examinations of head and neck, n.e.c.	330
Thorax	(not given)
chest, photofluorographic	(not given)
chest, radiographic	44
shoulder	260
thoracic spine and cervical spine	980
exams of chest or thorax, n.e.c.	1,520
Abdomen	960
Upper abdomen	960
cholecystography or cholangiogram	620
lumbar spine or dorsolumbar spine	1,920
upper gastrointestinal series	710
gastrointestinal, n.e.c.	920
upper abdomen, n.e.c.	1,240
Lower abdomen	970
barium enema	1,320
abdomen, KUB, flat plate	670
intra or retrograde pyelogram	590

Appendix A, cont.

Type of Examination	Milliroentgens (at skin entrance)
Lower abdomen, cont.	
pelvis or lumbo-pelvic	610
lumbosacral or sacral spine	2,180
hip	560
lower abdomen, n.e.c.	850
Extremities	100
Upper extremities	90
hand and/or wrist	100
forearm or elbow	60
upper extremities, n.e.c.	90
Lower extremities	110
ankle	140
foot and toes or heel	120
knee	110
tibia and fibula	40
femur or entire leg	120
lower extremities, n.e.c.	140
More than one body area	500

Appendix B
Nationwide Evaluation of X-Ray Trends
Weighted mean indexes by type of exam/projection

Type of exam/projection	Exposure at skin entrance (mR)
Chest (P/A)	23.0
Skull (Lateral)	276.0
ABD. (KUB) (A/P)	652.9
Retr. Pyelo. (A/P)	847.9
Thor. Spine (A/P)	851.3
Cervical Spine (A/P)	302.9
Lum - Sac Spine (A/P)	888.6
Full Spine (A/P)	306.6
Feet (D/P)	202.5
Dental B.W. Post	506.8
Dental Periapical	698.3
Dental Ceph. (Lateral)	31.8

MHD 182 X-Ray Uses

(a) Healing Arts

(1) Fluoroscopic

(aa) Equipment

(i) The protective tube housing shall be of the diagnostic type.

(ii) The target-to-panel or target-to-tabletop distance shall not be less than 12 inches.

(iii) The exposure switch shall be of the dead-man type.

(iv) A manually reset cumulative timing device activated by the fluoroscope exposure switch shall be used which will either indicate elapsed time by an audible signal or turn off the apparatus when the total exposure exceeds a predetermined limit in 1 or in a series of exposures not exceeding 5 minutes.

(v) The total filtration permanently in the useful beam shall not be less than 2.5 millimeters aluminum equivalent. When the table-top or panel surface is interposed between the source and the patient, its aluminum equivalent may be included as part of the total filtration. This requirement shall be assumed to have been met if the half-value layer is not less than that shown in the following table:

Operating Voltage (kVp)	Half-Value layer (millimeters aluminum)
80	2.4
90	2.6
100	2.8
120	3.1

(vi) The useful beam shall be attenuated by a primary barrier which shall be either:

(A) The fluoroscopic screen glass and frame which shall be the equivalent of 1.5 millimeters of lead shielding for voltages up to 100 kilovolts peak, 1.8 millimeters of lead shielding for voltages greater than 100 kilovolts peak but less than 125 kilovolts peak, and 2.0 millimeters for voltages 125 kilovolts peak or greater.

(B) The image intensification mechanism.

(vii) Collimators shall be provided to restrict the size of the useful beam to less than the area of the primary barrier, irrespective of the panel-to-screen distance. During fluoroscopy with image intensifiers, the useful beam shall not exceed the diameter of the input phosphor. Collimators, adjustable diaphragms, and shutters shall provide the same degree of protection as is required of the tube housing.

(viii) The tube mounting and the primary barrier shall be so linked together that the barrier always intercepts the useful beam. Exposure shall terminate if the primary barrier is removed from the useful beam. The unit shall be nonoperable without the primary barrier in place.

(ix) The screen shall be protected by a light-proof and dust-proof cover when the screen is not in use.

(x) A shielding device of at least 0.25 millimeter lead equivalent for covering the bucky slot during fluoroscopy shall be provided.

(xi) Devices which indicate the x-ray tube potential and current shall be provided.

(xii) Flexible leaded flaps which are the equivalent of 0.25 millimeter of lead shielding and which are hung from the screen shall be provided. The fluoroscopist shall wear a lead apron which is the equivalent of 0.25 millimeter of lead shielding.

(bb) **Structural Shielding.** All provisions of MHD 181 (i) (2) shall apply except that only secondary barriers shall be required.

(cc) **Operating Conditions**

(i) The exposure rate measured at the panel or tabletop shall be as low as practicable but shall not exceed 10 roentgens per minute.

(ii) With the fluorescent screen 14 inches (35 centimeters) from the panel or tabletop, the exposure rate 2 inches (5 centimeters) beyond the viewing surface of the screen shall not exceed 30 milliroentgens per hour for each roentgen per minute at the tabletop with the screen in the useful beam without a patient and with the fluoroscope operating at the highest potential employed.

(iii) The fluoroscopist shall wear a pair of protective gloves of at least 0.25 millimeter lead equivalent when the hands are used in the primary unattenuated beam or on the patient.

(iv) Extraneous light that interferes with the fluoroscopic examination shall be eliminated.

(v) The fluoroscopist's eyes shall be sufficiently dark-adapted for the visual task required before commencing fluoroscopy. Wearing red goggles for 10 minutes will usually satisfy adaptation requirements. Dark adaptation normally is not necessary when image intensifiers are used.

(dd) **Mobile Fluoroscopic Equipment.** Mobile fluoroscopic equipment shall meet the requirements of MHD 182 (a) (1) (aa) and (bb) where applicable, except that:

(i) In the absence of a tabletop, a cone or spacer frame shall limit the target-to-skin distance to not less than 12 inches.

(ii) Image intensification shall always be provided.

(iii) It shall be impossible to operate mobile fluorscopic equipment unless the useful beam is intercepted by the image intensifier.

(2) **Radiographic Installations Other than Dental, Veterinary Medicine, and Industrial**

(aa) **Equipment**

(i) The protective tube housing shall be of the diagnostic type.

(ii) Suitable devices (diaphragms, cones, adjustable collimators) capable of restricting the useful beam to the area of clinical interest shall be provided to define the beam and shall provide the same degree of attenuation as that required of the tube housing. Such devices shall be calibrated in terms of the size of the projected useful beam at all utilized focal spot to film distances.

(iii) Radiographic equipment, particularly multipurpose machines, should be equipped with adjustable collimators containing light localizers that define the entire field. Rectangular collimators are usually preferable. The field size indication on adjustable collimators shall be accurate to within

1 inch for a source-film distance of 72 inches. The light field shall be aligned with the x-ray field with the same degree of accuracy. The size of the x-ray beam projected by fixed aperture cones and collimators shall not exceed the dimensions of the x-ray film by more than 2 inches for a source-film distance (SFD) of 72 inches or 1 inch for a source-film distance of 36 inches.

(iv) Ruled scales shall be aligned both on the machine and beside the chest cassette holder to aid in accurately positioning the tube. A light beam indicator or a coupling device may be used in place of ruled scales.

(v) The aluminum equivalent of the total filtration in the useful beam shall be not less than that shown in the following table:

Operating Kilovolts Peak	**Minimum Total Filtration (inherent plus added)**
Below 50	0.5 millimeter aluminum
50-70	1.5 millimeters aluminum
Above 70	2.5 millimeters aluminum

The above requirements for filtration shall be assumed to have been met if the half-value layer is not less than that shown in the following table:

Operating Voltage (kVp)	**Half-Value layer (millimeters aluminum)**
49	0.6
70	1.6
90	2.6
100	2.9
110	3.1
120	3.4

(vi) A device shall be provided to terminate the exposure after a preset time or exposure.

(vii) A dead-man type of switch shall be so arranged that it cannot be conveniently operated from a position outside a shielded area. Exposure switches for spot film devices used in conjunction with fluoroscopic tables are exempted from this shielding arrangement.

(viii) The control panel shall include a device (usually a milliammeter) to give positive indication of the production of x rays whenever the x-ray tube is energized. The control panel shall include devices (labelled control settings and/or meters) indicating the physical factors (such as kilovolts peak, milliamperage, exposure time, or whether timing is automatic) used for the exposure.

(bb) **Structural Shielding.** In addition to the requirements of MHD 181 (i) (2) the following apply:

(i) All wall, floor, and ceiling areas exposed to the usful beam shall have primary barriers. Primary barriers in walls shall extend to a minimum height of 84 inches from the floor.

(ii) Secondary barriers shall be provided in all wall, floor, and ceiling areas not having primary barriers or where the primary barrier requirements are lower than the secondary barrier requirements.

(iii) The operator's station at the control shall be behind a protective barrier, either in a separate room, in a protected booth, or behind a shield which will intercept the useful beam and any radiation which has been scattered only once.

(iv) A lead glass window with a lead-equivalence equal to that of the adjacent barrier or a mirror system shall be provided large enough and so placed that the operator can see the patient without having to leave the protected area during exposure.

(v) Radiographic x-ray units powered equivalent to dental units shall meet the same shielding requirements as MHD 182 (a) (5) (bb) and MHD 182 (a) (8) (bb).

(cc) **Operating Procedures**

(i) No individual occupationally exposed to radiation shall be permitted to hold patients during exposures except during emergencies, nor shall any individual be used regularly for this service. Anyone holding a patient during x-ray exposures shall wear a protective apron and protective gloves of at least 0.25 millimeter of lead equivalence. He shall be so positioned that no part of his body will be struck by the useful beam.

(ii) Only individuals required for the radiographic procedure shall be in the radiographic room during exposures. Except for the patient, no parts of their bodies shall be in the useful beam. The useful beam shall be restricted to the area of clinical interest.

(iii) Adults of reproductive age and children should be provided with gonadal protection of a least 0.25 millimeter of lead equivalent when appropriate.

(3) **Special Requirements for Mobile Diagnostic Radiographic Equipment Other than Dental, Veterinary Medicine, and Industrial**

(aa) **Equipment**

(i) All requirements of MHD 182 (a) (2) (aa) apply except MHD 182 (a) (2) (aa) (iii) and MHD 182 (a) (2) (aa) (vi).

(ii) The exposure control switch shall be of the dead-man type and shall be so arranged that the operator can stand at least 6 feet from the patient and well away from the useful beam.

(iii) A light beam indicator shall be used to aid in accurately positioning the tube.

(bb) **Structural Shielding.** When a mobile unit is used routinely in one location, it shall be considered a fixed installation subject to the shielding requirements specified in MHD 181 (i) (2) and MHD 182 (a) (2) (bb).

(cc) **Operating Procedures**

(i) All provisions of MHD 182 (a) (2) (cc) apply except MHD 182 (a) (2) (cc) (ii).

(ii) Inherent provision shall be made so that the equipment is not operated at source-skin distances of less than 12 inches.

(iii) Personnel monitoring shall be required for all individuals operating mobile x-ray equipment.

(iv) Protective lead aprons of at least 0.25 millimeter of lead equivalence shall be worn by operators of mobile radiographic equipment.

(4) **Special Requirements for Chest Photofluorographic Installations**

(aa) **Equipment.** All provisions of MHD 182 (a) (2) (aa) apply except that a collimator shall restrict the useful beam to the area of the photofluorographic screen and a movable tube housing shall be coupled to the screen.

(bb) **Structural Shielding.** All provisions of MHD 181 (i) (2) and MHD 182 (a) (2) (bb) apply.

(cc) **Operating Procedures**

(i) All provisions of MHD 182 (a) (2) (cc) apply.

(ii) All individuals except the patient being examined shall be in shielded positions during exposures.

(iii) Personnel monitoring shall be required for all individuals operating the equipment and for clerical assistants in the controlled area.

(5) **Dental Radiographic Installations**

(aa) **Equipment**

(i) The tube housing shall be of diagnostic type.

(ii) Diaphragms or cones shall be used for collimating the useful beam and shall provide the same degree of protection as the housing. The diameter of the useful beam at the cone tip shall not be more than 2¾ inches for intra-oral radiography. With rectangular collimation, the longer side of the rectangle shall not exceed 2 inches.

(iii) Only open-end shielded cones shall be used after January 1, 1975.

(iv) A cone or spacer frame shall provide a target-to-skin distance of not less than 7 inches with apparatus operating above 50 kilovolts peak or 4 inches with apparatus operating at 50 kilovolts peak or below.

(v) The aluminum equivalent of the total filtration in the useful beam shall be not less than that shown in the following table:

Operating Kilovolts Peak	**Minimum Total Filtration (inherent plus added)**
At or Below 70	1.5 millimeters aluminum
Above 70	2.5 millimeters aluminum

The above requirements for filtration shall be assumed to have been met if the half-value layer is not less than that shown in the following table:

Operating Voltage (kVp)	**Half-Value layer (millimeters aluminum)**
At or Below 70	1.5
Above 70	2.5

(vi) A device shall be provided to terminate the exposure after a preset time or exposure.

(vii) The exposure control switch shall be of the dead-man type.

(viii) Each installation shall be provided with a protective barrier for the operator or shall be so arranged that the operator can stand at least 6 feet from the patient and well away from the useful beam.

(ix) Mechanical suport of the tube head and pointer cone shall maintain the exposure position without drift or vibration.

(x) The x-ray control panel shall include means for indication of:

(A) Tube voltage, (B) tube current (mA), and (C) exposure duration. The control panel should be so placed that the magnitude of these factors can be observed during the exposure procedure. The tube voltage and milliamperage shall be indicated by meters or by control settings. A milliammeter, a light or other device shall give visual indication when x rays are being produced.

(bb) **Structural Shielding.** In addition to the requirements of MHD 182 (a) (8) (bb):

(i) Dental rooms containing x-ray machines shall be provided with primary barriers at all areas struck by the useful beam. In many cases structural materials of ordinary walls suffice as a protective barrier without addition of special shielding material.

(ii) When dental x-ray units are installed in adjacent rooms or areas, protective barriers shall be provided between the rooms or areas.

(cc) **Operating Procedures**

(i) The exposure at the tip of the pointer cone shall be as low as practicable and shall not exceed 0.8 roentgen per film for intra-oral radiography.

(ii) Neither the dentist nor his assistant shall be permitted to hold patients or films during x-ray exposures, nor shall any individual be regularly used for this purpose.

(iii) During each x-ray exposure the operator shall stand at least 6 feet from the patient or behind a protective barrier.

(iv) Only the patient shall be in the useful beam.

(v) Neither the tube housing nor the pointer cone shall be hand held during x-ray exposures by anyone.

(vi) Fluoroscopy shall not be used in dental examinations.

(vii) Adults of reproductive age and children shall be provided with gonadal protection when a full mouth series of exposures are made with intra-oral radiography.

(dd) **Panoramic Installations.** This section applies to those installations which consist of a tube head with a collimator providing a narrow (1-2 mm) useful beam and an extra-oral film carrier which are interlocked in their motion about the patient. Such equipment shall meet the requirements of MHD 182 (a) (5) (aa) (i), (5) (aa) (ii), (5) (aa) (v), (5) (aa) (vii), and (5) (aa) (x). While the narrow useful beam and the shielding of the film carrier reduce the need for structural shielding and operator protection, the guidance of a qualified expert should be sought whenever high workloads are anticipated; for example, in x-ray surveys of large numbers of persons in succession.

(6) **Therapeutic X-Ray Installations**

(aa) **Equipment**

(i) The protective tube housing shall be of the therapeutic type.

(ii) Permanent diaphragms or cones used for collimating the useful beam shall afford the same degree of protection as the tube housing. Adjustable or removable beam-defining diaphragms or cones shall transmit not more than 5 percent of the useful beam obtained at the maximum kilovoltage and with maximum treatment filter.

(iii) Filters shall be secured in place to prevent them from dropping out during treatment. The filter slot shall be so constructed that the radiation escaping through it does not exceed 1 roentgen per hour at 1 meter, or, if the radiation from the slot is accessible to the patient, 30 roentgens per hour at 5 centimeters from the external opening.

(iv) A filter identification system shall be used on all therapy machines with changeable filters. The filter(s) shall be clearly visible for easy recognition by the operator from his position at the controls or the presence or absence of any filter shall be indicated at the control panel designed to permit easy recognition of the specific filter in place.

(v) The x-ray tube shall be so mounted that it cannot turn or slide with respect to the aperture.

(vi) Means shall be provided to immobilize the tube housing during stationary portal treatment.

(vii) A suitable exposure control device (e.g., an automatic timer, exposure meter or dose meter) shall be provided to terminate the exposure after a preset time interval or preset exposure or dose limit. Means shall also be provided for the operator to terminate the exposure at any time.

(viii) Equipment utilizing shutters to control the useful beam shall have a shutter position indicator on the control.

(ix) There shall be on the control panel an easily discernible indicator which will give positive information as to whether or not the x-ray tube is energized.

(x) Operating units shall not be left unattended at any time.

(bb) **Structural Shielding.** In addition to the requirements of MHD 181 (i)(2):

(i) All wall, floor, and ceiling areas that can be struck by the useful beam, plus a border of 1 foot, shall be provided with primary protective barriers based on use factors involved.

(ii) All wall, floor, and ceiling areas that, because of restrictions in the orientation of the useful beam, will not be struck by the useful beam shall be provided with secondary barriers.

(iii) With equipment operating above 125 kilovolts peak, the required barriers shall be an integral part of the building.

(iv) With equipment operating above 150 kilovolts peak, the control station shall be within a protective booth or outside the treatment room.

(v) Interlocks shall be provided for x-ray therapy equipment capable of operating above 150 kilovolts peak so that when any door of the treatment room is opened, either the machine will shut off automatically or the radiation level within the room will be reduced to an average of not more than 2 milliroentgens per hour and a maximum of 10 milliroentgens per hour at a distance of 1 meter in any direction from the target. After shut off or reduction in exposure rate, restoration of the machine to full operation shall be possible only from the control panel.

(vi) Provision shall be made to permit continuous observation of patients during irradiation.

(vii) Windows, mirror systems, or closed-circuit television viewing screens used for observing the patient shall be so located that the operator may see the patient and the control panel from the same position.

(viii) Means for aural communication between the patient and control room shall be provided (e.g., voice, buzzer).

(cc) **Operating Procedures**

(i) All new installations, and existing installations not previously surveyed, shall have a protection survey conducted by, or under the direction of, a person who by training and experience is qualified to evaluate such installation. A protection survey shall also be conducted following any change in the installation which might produce a radiation hazard. The surveyor shall report his findings in writing to the person in charge of the installation, a copy of which shall be made available to the Board.

(ii) The installation shall be operated in compliance with any limitations indicated by the protection survey.

(iii) If any individual is required to be in the treatment room with the patient during exposure because of clinical necessity, he shall be protected as much as possible from scattered radiation and shall not be in the useful beam. The individual so required shall not be one who is occupationally exposed to radiation and no individual shall be used regularly for this service. The exposure of any individual used for this purpose shall be monitored.

(iv) The output of each therapeutic x-ray machine shall be calibrated by, or under the direction of, a person who by training and experience is qualified to evaluate such installations. The calibration shall be repeated after any change in or replacement of components of the x-ray generating equipment which could cause a change in x-ray output. Check calibration shall be made at least once a year thereafter. Records of calibration shall be maintained by the registrant.

(7) **Special Requirements for X-Ray Therapy Equipment Operated at Potentials of 60 Kilovolts and Below**

(aa) **Equipment.** All provisions of MHD 182 (a) (6) (aa) apply with the following exception: Such x-ray therapy units which are used for "contact therapy" shall meet the additional requirement that the leakage radiation measured at 2 inches (5 centimeters) from the housing shall not exceed 0.1 roentgen per hour.

(bb) **Structural Shielding.** All requirements of MHD 181 (i) (2) shall apply.

(cc) **Operating Procedures**

(i) Automatic timers shall be provided which will permit accurate presetting and determination of exposure as short as 1 second.

(ii) In the therapeutic application of apparatus constructed with beryllium or other low-filtration windows, the registrant shall insure that the unfiltered radiation reaches only the part intended and that the useful beam is blocked at all times except when actually being used.

(iii) If the tube is hand held during irradiation, the operator shall wear protective gloves of at least 0.25 millimeter lead equivalence.

(8) **Veterinary Medicine Radiographic Installations**

(aa) **Equipment**

(i) The protective tube housing shall be of the diagnostic type.

(ii) Diaphragms or cones shall be provided for collimating the useful beam to the area of clinical interest and shall provide the same degree of protection as is required of the housing.

(iii) Except when contraindicated for a particular radiographic purpose, the total filtration permanently in the useful beam shall not be less than 1.5 millimeters aluminum equivalent for equipment operating at or below 70 kilovolts peak and 2.0 millimeters aluminum equivalent for machines operated in excess of 70 kilovolts peak.

(iv) A device shall be provided to terminate the exposure after a preset time or exposure.

(v) A dead-man type of exposure switch shall be provided together with an electrical cord of sufficient length so that the operator can stand out of the useful beam and at least 6 feet from the animal or behind a protective barrier during all x-ray exposures.

(bb) **Structural Shielding.** All wall, ceiling, and floor areas shall be equivalent to, or provided with, appropriate protective barriers as required in MHD 182 (a) (2) (bb).

(cc) **Operating Procedures**

(i) The operator shall stand well away from the tube housing and the animal during radiographic exposures. Provisions shall be made so that the operator will not be required to stand in the useful beam. Hand held fluoroscopic screens shall not be used. The tube housing shall not be held by the operator. No individual other than the operator shall be in the x-ray room while exposures are being made unless such individual's assistance is required or he is a student receiving instruction and the recommended protective procedures are followed.

(ii) In any procedure in which the operator or other assisting individual is not located behind a protective barrier, clothing consisting of a protective apron having a lead equivalent of not less than 0.25 millimeter shall be worn by the operator and any other individuals in the room during x-ray exposures.

(iii) No individual shall be regularly employed to hold or support animals or hold film during radiation exposures. Occupationally exposed individuals shall not perform the service except in cases in which no other method is available. Any individual holding or supporting an animal during radiation exposure shall wear protective gloves and apron having a lead equivalence of not less than 0.25 millimeter. No individual assisting as the film cassette holder shall have any portion of his body in the useful beam, including the hand inside the protective glove.

(b) **Industrial.** Industrial x-ray installations shall be classified as either class A, class B, class C, class D, or special class as specified by the registrant at the time of registration.

Class A permits unlimited use of maximum capacity.

Class B permits unlimited use under limited operating conditions.

Class C permits limited use under specified conditions.

Class D permits limited use and temporary operation and includes portable or mobile industrial x-ray installations.

Special class covers those installations which use x-ray devices for thickness measurements or coating weight determinations on continuously moving webs.

(1) Class A Installation Requirements

(aa) The x-ray source and the objects exposed to x rays must be contained within a permanent enclosure except as provided in MHD 182 (b) (1) (ee). The enclosure construction shall attenuate the primary and secondary radiation so that the exposure rate at any accessible external point shall not exceed 2 milliroentgens per hour when:

(i) The x-ray beam is adjusted to give maximum exposure rate with the x-ray generator at maximum.

(ii) The x-ray tube is placed in the shortest tube-to-wall radiographically useable position.

(bb) Reliable interlocks shall be provided which will prevent entering of the enclosure while the x-ray generator is in operation or will terminate the generation of x rays should the enclosure be opened.

(cc) Persons shall at all times be able to escape from the enclosure.

(dd) The enclosure shall be equipped with visible and/or audible signals. Such signals shall be activated upon generation of x rays and shall remain activated continually while x rays are being generated.

(ee) If the ceiling barrier does not attenuate the exposure rate as set forth in MHD 182 (b) (1) (aa), a posted barrier such as a fence shall be used to restrict access to the ceiling area.

(ff) No person shall be permitted to remain within the enclosure while the x-ray generator is in operation.

(gg) No x-ray apparatus or other radiographic unit shall be left unattended without either the apparatus being locked in an inoperable condition or the room or building in which the apparatus is located being locked in a manner which will prevent its use by unauthorized personnel.

(hh) All protective enclosures and equipment shall be kept in good condition.

(2) Class A Operating and Emergency Procedures

(aa) A written manual of operating and emergency procedures shall be in the possession of the operator and the person responsible for each installation. The operating procedures shall be so designed that every practicable means have been employed to minimize exposure and that no person is likely to be exposed to radiation doses that exceed the maximum permissible doses specified in Table 1 of the Appendix.

(bb) The Board shall be notified in the event of an accident resulting in a possible or actual exposure of a person in excess of the design basis specified in MHD 182 (b) (2) (aa) above.

(cc) A radiation protection survey shall be performed when changes have been made in shielding, operation, or equipment. The installation shall be checked periodically for unknown changes and malfunctioning equipment.

(dd) Records shall be maintained of each radiation protection survey and such records shall be available to the Board or its authorized agents.

(ee) Utilization logs showing the voltage, current, and exposure time for each radiographic exposure shall be maintained.

(3) **Class B Installation Requirements and Operating and Emergency Procedures**

(aa) All requirements of MHD 182 (b) (1) and (2) apply.

(bb) The controls for the kilovoltage and milliamperage shall be limited by mechanical or electrical means so that the maximum normal operating conditions specified by the registrant at the time of registration cannot be exceeded.

(4) **Class C Installation Requirements and Operating and Emergency Procedures.** All requirements of MHD 182 (b) (1) and (2) apply except that:

(aa) An exposure rate of 50 milliroentgens per hour at accessible external points is allowable.

(bb) The workload of the machine shall be restricted so that the cumulative exposure at any accessible point outside the protective enclosure does not exceed 100 milliroentgens in any 7 consecutive days.

(cc) The number of hours per day or week for permissible operation shall be stated on the registration form.

(dd) Warning signs shall be posted in those areas outside the protection barriers in which the exposure rate at any accessible external point exceeds 2 milliroentgens per hour with the generator operating at its maximum capacity. A visible and/or audible signal shall be provided within the posted area which shall be activated during the generation of x rays.

(ee) Continuous personnel monitoring shall be enforced for all personnel in the posted area at all times.

(5) **Class D Installation Requirements and Operating and Emergency Procedures.** An x-ray installation not meeting the requirements for class A, class B, or class C installation may be operated for a period of 30 days provided the requirements listed below are met. When the 30-day period is impractical or when an undue and unnecessary hardship is involved, the period may be extended by the Board.

(aa) All provisions of MHD 182 (b) (2) apply.

(bb) No x-ray apparatus shall be left unattended without either the apparatus being locked in inoperable condition or the room or building in which the apparatus is located being locked in a manner which will prevent its use by unauthorized personnel.

(cc) All areas in which the exposure rates exceed 5 milliroentgens per hour shall be posted and barricaded by a fence, rope, or other suitable personnel barriers erected outside the 5 milliroentgens per hour iso line.

(dd) Continuous personnel monitoring shall be enforced for individuals in the posted areas and such other persons who may be specified by the Board.

(ee) A calibrated and operable survey instrument shall be available at each installation. The instrument shall have a range such that 2 milliroentgens per hour through 1 roentgen per hour can be measured.

(ff) The initial registration shall be in the possession of the Board 3 days before the unit is operated at any location.

(gg) If the unit has been previously registered and is moved to a new address, the Board shall be in possession of the notification of a change in work address prior to use of the source at any address other than that indicated on the registration form.

(6) **Special Class — X-Ray Thickness Gauge Installation Requirements**

(aa) The x-ray source and the materials exposed to x rays must be contained within a permanent enclosure. The enclosure construction shall attenuate the primary and secondary radiation so that the exposure rate through any portion of the shielding is less than 0.5 milliroentgen per hour and the exposure rate through openings in the shielding is less than 5 milliroentgens per hour at any accessible external point when the equipment is being operated at its maximum potential.

(bb) Reliable interlocks shall be provided on access doors in the primary and secondary shielding which will terminate the generation of x rays or attenuate the radiation exposure rate to 5 milliroentgens per hour should the enclosure be opened.

(cc) The enclosure shall be equipped with visible signals. Such signals shall be activated upon generation of x rays and shall remain activated continually while x rays are being generated. If the x-ray source has a shutter, the enclosure shall also be equipped with a visible signal indicating whether the shutter is open or closed.

(7) **Special Class Operating and Emergency Procedures.** All requirements of MHD 182 (b) (2) apply except MHD 182 (b) (2) (ee).

MHD 183 Radium Uses

(a) **Healing Arts.** The following special provisions of this part apply to all registrants who use radium in the healing arts and are in addition to, and not in substitution for, other applicable provisions of the regulations.

(1) **Source Custodian**

(aa) Every hospital, clinic, or physician's office in which a person owns or rents radium sources shall designate a source custodian.

(bb) The source custodian shall have the necessary training, experience, and inherent or delegated authority to exercise adequate control over the use and accountability of sources.

(cc) The name of the source custodian shall be submitted to the Board.

(2) **Accountability, Storage, and Transit**

(aa) The source custodian shall provide accountability of radium sources and shall keep a permanent record of the issue and return of all radium sources.

(bb) When not in use radium sources and applicators containing radium sources shall be kept in a protective enclosure of such material and wall thickness as is necessary to assure that the appropriate limits of radiation will not be exceeded.

(cc) For local transportation the container shall have sufficient shielding to assure that the appropriate limits of radiation are not exceeded.

(dd) Transportation of radium off the premises shall be in accordance with Title 49, Parts 71-78 of the Code of Federal Regulations or Title 14, Part 103, Chapter 1 of the Code of Federal Regulations, or with Post Office Department Regulations, whichever is applicable.

(3) **Use and Procedure**

(aa) The registrant shall demonstrate to the Board upon request that the proposed methods of use are consistent with the policy of minimization and are not likely to cause any individuals other than the patient receiving therapy to receive a dose in excess of the maximum permissible dose equivalents.

(bb) The registrant shall insure that:

(i) During each radiotherapeutic operation unauthorized entry into a radiation area shall be prevented.

(ii) The patient's room shall be identified as a radiation area and all individuals entering the room shall comply with the requirements of MHD 181 (c) (2).

(iii) The preparation and dismantling of radium applicators or similar procedures shall be performed behind adequate protective shields. Protective windows or mirror shall be provided for viewing purposes.

(iv) Remote handling equipment such as tongs and forceps shall be used for all radium sources. Under no circumstances shall a source be touched by the fingers.

(v) Loss of radium sources shall be reported to the Board in accordance with MHD 181 (g).

(4) **Testing Radium Sources for Leakage and Contamination**

(aa) The registrant shall provide for testing for leakage and contamination prior to initial use.

(bb) All radium sources shall be tested for leakage every 6 months.

(cc) If there is reason to suspect that a sealed source has been damaged, it shall be tested for leakage before further use.

(dd) Leak tests shall be capable of detecting the presence of 0.005 microcurie of contamination on the radium source.

(ee) Leakage of radium sources shall be reported within 24 hours of discovery to the Board.

(ff) Any test conducted pursuant to these regulations which indicates the presence of 0.005 microcurie or more of contamination shall be considered evidence that the radium source is leaking and the registrant shall immediately withdraw the source from use.

(gg) All leaking sources shall be decontaminated and re-encapsulated or disposed of in accordance with MHD 183 (c).

(b) **Industrial Radium Installation.** The regulations hereunder establish radiation safety requirements for sealed radium sources utilized for industrial radiography. Nothing in MHD 183 (b) shall apply to uses of radium sources in the healing arts.

(1) The registrant shall provide accountability of sealed sources and shall keep a permanent record of the issue and return of all sealed sources.

(2) The registrant shall assure adequate shielding and housing of the source.

(aa) When not in use, sealed sources shall be kept in a protective enclosure of such material and wall thickness as is necessary to limit doses to those permitted under these regulations.

(bb) Source housing shall provide the following:

(i) If the source is permanently mounted in a housing with a beam control device or extended from and retracted into a housing, this device shall be of positive design capable of acting regardless of the position of the housing.

(ii) It shall be possible to move the source to a shielded position manually with a minimum risk of exposure in the event of the failure of the automatic mechanism.

(iii) Warning devices on the housing and the control panel shall plainly indicate whether the apparatus is "on" or "off."

(cc) Transfer of the source shall be performed according to the following:

(i) If the apparatus is of a type in which the source is removed from the shield when in use, transfer shall be accomplished by a remote control mechanism.

(ii) Transfer mechanisms shall be designed to minimize the possibility of damage to the source in transit.

(dd) Each radiographic exposure device shall be provided with a lock within the enclosure. The enclosure shall also be provided with a lock and shall be kept locked at all times except when under the direct surveillance of the industrial radiographer or his assistant.

(ee) Sources shall have leak tests performed as follows:

(i) The registrant shall provide for testing for leakage and contamination prior to initial use.

(ii) All sealed radium sources shall be tested for leakage at least every 6 months.

(iii) If there is reason to suspect that a sealed source has been damaged, it shall be tested for leakage before further use.

(iv) Leak tests shall be capable of detecting the presence of 0.005 microcurie of contamination of radium and its decay products.

(v) Any tests conducted which reveal the presence of 0.005 microcurie or more of removable contamination shall be considered evidence that the sealed source is leaking and the registrant shall withdraw the source from use and shall cause it to be decontaminated and resealed or to be disposed of in accordance with MHD 183 (c).

(vi) Leaking or lost sources shall be reported to the Board in accordance with MHD 181 (g).

(ff) A radiation survey shall be made after each use to determine that the radium source has been returned to its shielded position. Records shall be kept of each survey for inspection by the Board.

(c) **Waste Disposal of Radium Sources**

(1) Radium sources considered to be waste shall be disposed of through one of the following:

(aa) A radium collection agency

(bb) A private radium collection company

(cc) An institution that has suitable waste disposal facilities.

(2) The delivery of radium waste to the receiver shall be in accordance with MHD 181 (f).

MHD 184 Special Uses of Electric Equipment

(a) **Accelerators, X-Ray Diffraction Units, and Electron Microscopes.** Accelerators, x-ray diffraction units, and electron microscopes shall be installed, shielded, and operated in such a manner that no one shall be exposed beyond the appropriate limits as defined in MHD 181 (c) (2).

(b) **Television Receivers.** No television receivers shall be manufactured, sold, demonstrated or otherwise distributed unless they are in conformity with the Code of Federal Regulations, Title 42, Part 78.

(c) **Research and Teaching Institutions.** The following special provisions of this part apply to all registrants who use ionizing radiation in research and teaching institutions and are in addition to, and not in substitution for, other applicable provisions of these regulations.

(1) The possession by secondary or elementary schools of radium-226 in excess of those quantities exempted in MHD 181 (d) (1) (Table 3) shall be prohibited.

(2) The use of registerable sources of ionizing radiation in secondary or elementary schools is limited to registrants specifically designated by the Board or licensed by the U. S. Atomic Energy Commission to use by-product materials. The Board may authorize a registrant to use sources of ionizing radiation if the registrant demonstrates sufficient knowledge of radiation protection and if applicable principles of radiation protection have been implemented in the physical construction and/or preparation of the source.

(3) Students under 18 years of age shall not receive in any period of one calendar quarter a whole body exposure exceeding 10 percent of the limits specified in Table 1 in the Appendix.

MHD 185 Nuclear Facilities. Regulation 11040(i) "Nuclear reactors and facilities," **Minnesota State Board of Health Regulations on Ionizing Radiation** adopted by Minnesota State Board of Health December 4, 1958 is renumbered here to be in accordance with the numbering system chosen for the revised regulations on ionizing radiation. The regulation is as follows:

1. The term "nuclear reactor" as used herein means any installation, machine, device, or assemblage or collection of installations, machines, or devices that does or is intended or designed to contain a controlled self-sustaining neutron chain reaction. The term "facility" as used herein includes nuclear reactors and also includes any plant, installation, or device for processing or reprocessing nuclear fuel, and any plant, installation, device, place, or location for disposal of radioactive wastes or for temporary or permanent disposal of radioactive materials, equipment, or nuclear fuel.

2. Before the construction of any nuclear reactor or facility is started within this State a general description thereof shall be submitted to the Board of Health containing such information as may be necessary or appro-

priate to a determination of any actual or potential hazard to or effect upon the public health, and specifying the following information: (aa) the name, address and corporate or individual character of the person who will own the facility, and, if different, of the person who will operate it; (bb) the name and address of the principal contractors who will construct the facility; (cc) a description of the general character of the means employed to utilize nuclear energy; (dd) a statement as to the character, quantity and source of the materials that will be utilized as a source of nuclear energy; (ee) a description of the precise location of the facility with reference to any relevant known topographical, subsurface, or meteorological features of the location, such as adjacent bodies of water; (ff) a statement as to plans for monitoring levels of radioactivity in the various phases of the environment; (gg) a statement as to the anticipated quantity and means of storage and disposition of any radioactive waste materials that will result from the operation; (hh) a preliminary statement as to the standards and measures that will be employed to ensure the safety of personnel employed in or near the proposed facility; (ii) a preliminary statement as to the standards and measures that will be employed to prevent radioactive contamination of air, water, and other elements of the environment; (jj) a preliminary statement specifying in standard scientific terms and quantitative units the nature and amount of radioactivity that will be permitted to pass into the environmental air, water, and other elements within a specified period of time, stating in what manner and form such radioactivity will be permitted to pass into the environment and describing the safety checks that will be employed to ensure that no larger quantity of radioactivity escapes into the environment, and (kk) a preliminary description of the maximum credible accident which might occur at the proposed facility and how it will be controlled, together with any information relevant to a complete hazard report.

3. No part of the construction of a nuclear reactor or facility shall be started within this State without the express approval of the Board of Health until 30 days after the submission to it of such description and information. Within 30 days after such submission the Board of Health, or its duly authorized agents, may require the submission of additional information relating to any specific matter referred to herein, and the Board of Health, or its duly authorized agents, may object to any part of the proposed design, description, plans, method of operation, standards or safety measures, upon the grounds that the public health is endangered, and may require such modification in such design, plans, method of operation, standards or safety measures as will eliminate the danger to the public health. In the event that within 30 days after the submission to it of the description, information, design and plans for a proposed nuclear reactor or facility the Board of Health does not object to any part thereof, the facility may be constructed in accordance with the description, design, and plans submitted to the Board of Health.

4. If there is any substantial deviation from or change in the description, design, or plans as submitted to the Board of Health, full information relating to such deviation or change shall be submitted to the Board of Health immediately.

5. The Board of Health shall be notified of the date when it is proposed that a nuclear reactor shall be put into operation. Such notification shall specify any deviations from, or changes in, the description, design, or plans as previously submitted to the Board of Health and the facility as actually

constructed. At least 30 days, and not more than 60 days, prior to this proposed date, the owner of the reactor shall apply to the Board of Health for its approval to operate the facility. No reactor shall be operated in this State until the owner has received, and is in the possession of, such an approval.

6. Whenever it is proposed to alter, enlarge, move, or substantially modify or change any existing nuclear reactor or facility, the description, design, and plans of such proposed alteration, enlargement, move, modification or change shall be submitted to the Board of Health at least 30 days prior to the time that it is proposed to initiate such work, and these regulations shall apply to any substantial alteration or enlargement as though such work were the construction of a new facility.

7. The operator of each nuclear reactor or facility within this State shall report to the Board of Health at least annually, stating the measures that have been taken during the preceding year to monitor and measure the nature and amount of radioactivity discharged or allowed to escape into the environment from such facility, and stating in standard scientific terms and quantitative units the nature and quantity of radioactivity that has been discharged or allowed to escape into the environment during the preceding year.

8. When an accident or other situation occurs in this State in the operation of a nuclear reactor or facility which results or threatens to result in the radioactive contamination of a person, animal, or the environment, or the exposure of a person to, or the escape into the environment of, ionizing radiation in a manner or to a degree or in a quantity different or greater than specified in the description and information last previously filed with the Board of Health, it shall be the duty of the owner and operator and of the person then in charge of such facility to have notification of such occurrence communicated to the Board of Health by telephone immediately upon the discovery of the facts, and to have all facts and circumstances of the occurrence reported in detail in writing to the Board of Health within seven days thereafter.

9. Any facility in design or under construction as of January 1, 1959, shall not be exempt from the provisions of these regulations.

APPENDIX

Table 1 ....Maximum Permissible Doses (Dose Equivalents)
Table 2 ....Neutron Flux Dose Equivalents
Table 3 ....Registration Exemption Possession Limits
Table 4 ....Exempt Concentrations

Table 1

MAXIMUM PERMISSIBLE DOSES (DOSE EQUIVALENTS)

	Average weekly dose[a]	Maximum 13-week dose	Maximum yearly dose	Maximum accumulated dose[c]
Occupational Personnel	rem[b]	rem[b]	rem[b]	rem[b]
Controlled areas—Occupational Dose				
Whole body, gonads, blood-forming organs, and lens of eye..........	0.1	1¼		5(N-18)
Skin of whole body..		7½	30	
Hands and forearms, head, neck, feet, and ankles..................	1.5	18¾	75	
Public				
Environs (Non-controlled areas)				
Nonoccupational Dose	0.01		0.5	

Notes:

N = Age in years and is greater than 18.

[a] For design purposes only.

[b] The dose in rems may be assumed to be equal to the exposure in röentgens for x and gamma rays.

[c] Where an employee's accumulative dose is partly due to radiation from isotopes and partly to radiation from x-ray units, the limits established in Table 1, would apply to the sum of the radiation doses.

Table 2

NEUTRON FLUX DOSE EQUIVALENTS

Neutron Energy (MeV)	Number of neutrons per square centimeter equivalent to a dose of 1 rem (neutrons/cm^2)	Average flux to deliver 100 millirem in 40 hrs. (neutrons/cm^2 per sec.)
Thermal	970 x 10^6	670
0.0001	720 x 10^6	500
0.005	820 x 10^6	570
0.02	400 x 10^6	280
0.1	120 x 10^6	80
0.5	43 x 10^6	30
1.0	26 x 10^6	18
2.5	29 x 10^6	20
5.0	26 x 10^6	18
7.5	24 x 10^6	17
10.0	24 x 10^6	17
10 to 30	14 x 10^6	10

Table 3

REGISTRATION EXEMPTION POSSESSION LIMITS

Material	Microcuries	Material	Microcuries
Americium 241	0.01	Cesium 136	10
Antimony 122	100	Cesium 137	10
Antimony 124	10	Chlorine 36	10
Antimony 125	10	Chlorine 38	10
Arsenic 73	100	Chromium 51	1,000
Arsenic 74	10	Cobalt 58m	10
Arsenic 76	10	Cobalt 58	10
Arsenic 77	100	Cobalt 60	1
Barium 131	10	Copper 64	100
Barium 140	10	Dysprosium 165	10
Bismuth 210	1	Dysprosium 166	100
Bromine 82	10	Erbium 169	100
Cadmium 109	10	Erbium 171	100
Cadmium 115m	10	Europium 152 9.2 h	100
Cadmium 115	100	Europium 152 13 yr	1
Calcium 45	10	Europium 154	1
Calcium 47	10	Europium 155	10
Carbon 14	100	Fluorine 18	1,000
Cerium 141	100		
Cerium 143	100	Gadolinium 153	10
Cerium 144	1	Gadolinium 159	100
Cesium 131	1,000	Gallium 72	10
Cesium 134m	100	Germanium 71	100
Cesium 134	1	Gold 198	100
Cesium 135	10	Gold 199	100

Table 3 (continued)

Material	Microcuries
Hafnium 181	10
Holmium 166	100
Hydrogen 3	1,000
Indium 113m	100
Indium 114m	10
Indium 115m	100
Indium 115	10
Iodine 125	1
Iodine 126	1
Iodine 129	0.1
Iodine 131	1
Iodine 132	10
Iodine 133	1
Iodine 134	10
Iodine 135	10
Iridium 192	10
Iridium 194	100
Iron 55	100
Iron 59	10
Krypton 85	100
Krypton 87	10
Lanthanum 140	10
Lutetium 177	100
Manganese 52	10
Manganese 54	10
Manganese 56	10
Mercury 197m	100
Mercury 197	100
Mercury 203	10
Molybdenum 99	100
Neodymium 147	100
Neodymium 149	100
Nickel 59	100
Nickel 63	10
Nickel 65	100
Niobium 93m	10
Niobium 95	10
Niobium 97	10
Osmium 185	10
Osmium 191m	100
Osmium 191	100
Osmium 193	100
Palladium 103	100
Palladium 109	100
Phosphorus 32	10
Platinum 191	100
Platinum 193m	100
Platinum 193	100
Platinum 197m	100
Platinum 197	100
Plutonium 239	0.01
Polonium 210	0.1
Potassium 42	10
Praseodymium 142	100
Praseodymium 143	100
Promethium 147	10
Promethium 149	10
Radium 226	10
Rhenium 186	100
Rhenium 188	100
Rhodium 103m	100
Rhodium 105	100
Rubidium 86	10
Rubidium 87	10
Ruthenium 97	100
Ruthenium 103	10
Ruthenium 105	10
Ruthenium 106	1
Samarium 151	10
Samarium 153	100
Scandium 46	10
Scandium 47	100
Scandium 48	10
Selenium 75	10
Silicon 31	100
Silver 105	10
Silver 110m	1
Silver 111	100
Sodium 24	10
Strontium 85	10
Strontium 89	1
Strontium 90	0.1
Strontium 91	10
Strontium 92	10
Sulphur 35	100
Tantalum 182	10
Technetium 96	10
Technetium 97m	100
Technetium 97	100
Technetium 99m	100

Table 3 (continued)

Material	Microcuries	Material	Microcuries
Technetium 99	10	Xenon 131m	1,000
Tellurium 125m	10	Xenon 133	100
Tellurium 127m	10	Xenon 135	100
Tellurium 127	100	Ytterbium 175	100
Tellurium 129m	10	Yttrium 90	10
Tellurium 129	100	Yttrium 91	10
Tellurium 131m	10	Yttrium 92	100
Tellurium 132	10	Yttrium 93	100
Terbium 160	10	Zinc 65	10
Thallium 200	100	Zinc 69m	100
Thallium 201	100	Zinc 69	1,000
Thallium 202	100	Zirconium 93	10
Thallium 204	10	Zirconium 95	10
Thorium (natural)	50	Zirconium 97	10
Thulium 170	10		
Thulium 171	10		
Tin 113	10		
Tin 125	10		
Tungsten 181	10		
Tungsten 185	10	Any alpha emitting radionuclide not listed above or mixtures of alpha emitters of unknown composition	0.01
Tungsten 187	100		
Uranium (natural)	50		
Uranium 233	0.01		
Uranium 234-Uranium 235	0.01		
Vanadium 48	10	Any radionuclide other than alpha emitting radionuclides not listed above or mixtures of beta emitters of unknown composition	0.1

Note: Where there is a combination of isotopes in known amounts the limit for the combination shall be derived as follows: Determine, for each isotope in the combination, the ratio between the quantity present in the combination and the limit otherwise established for the specific isotope when not in combination. The sum of such ratios for all the isotopes in the combination may not exceed "1" (i.e., "unity").

Example: If a particular batch contains 20,000 μCi of Au^{198} and 50,000 μCi of C^{14}, it may also include not more than 300 μCi of I^{131}. This limit was determined as follows:

$$\frac{20{,}000\ \mu\text{Ci Au}^{198}}{100{,}000\ \mu\text{Ci}} + \frac{50{,}000\ \mu\text{Ci C}^{14}}{100{,}000\ \mu\text{Ci}} + \frac{300\ \mu\text{Ci I}^{131}}{1{,}000\ \mu\text{Ci}} = 1$$

The denominator in each of the above ratios was obtained by multiplying the figure in the table by 1,000.

Table 4

EXEMPT CONCENTRATIONS

Element (atomic number)	Isotope	Column I Gas concentration μCi/ml[1]	Column II Liquid and solid concentration μCi/ml[2]
Antimony (51)	Sb 122		3x10^{-4}
	Sb 124		2x10^{-4}
	Sb 125		1x10^{-3}
Argon (18)	A 37	1x10^{-3}	
	A 41	4x10^{-7}	
Arsenic (33)	As 73		5x10^{-3}
	As 74		5x10^{-4}
	As 76		2x10^{-4}
	As 77		8x10^{-4}
Barium (56)	Ba 131		2x10^{-3}
	Ba 140		3x10^{-4}
Beryllium (4)	Be 7		2x10^{-2}
Bismuth (83)	Bi 206		4x10^{-4}
Bromine (35)	Br 82	4x10^{-7}	3x10^{-3}
Cadmium (48)	Cd 109		2x10^{-3}
	Cd 115m		3x10^{-4}
	Cd 115		3x10^{-4}
Calcium (20)	Ca 45		9x10^{-5}
	Ca 47		5x10^{-4}
Carbon (6)	C 14	1x10^{-6}	8x10^{-3}
Cerium (58)	Ce 141		9x10^{-4}
	Ce 143		4x10^{-4}
	Ce 144		1x10^{-4}
Cesium (55)	Cs 131		2x10^{-2}
	Cs 134m		6x10^{-2}
	Cs 134		9x10^{-5}
Chlorine (17)	Cl 38	9x10^{-7}	4x10^{-3}
Chromium (24)	Cr 51		2x10^{-2}
Cobalt (27)	Co 57		5x10^{-3}
	Co 58		1x10^{-3}
	Co 60		5x10^{-4}
Copper (29)	Cu 64		3x10^{-3}
Dysprosium (66)	Dy 165		4x10^{-3}
	Dy 166		4x10^{-4}
Erbium (68)	Er 169		9x10^{-4}
	Er 171		1x10^{-3}
Europium (63)	Eu 152 (T/2=9.2 Hrs.)		6x10^{-4}
	Eu 155		2x10^{-3}
Fluorine (9)	F 18	2x10^{-6}	8x10^{-3}
Gadolinium (64)	Gd 153		2x10^{-3}
	Gd 159		8x10^{-4}
Gallium (31)	Ga 72		4x10^{-4}
Germanium (32)	Ge 71		2x10^{-2}

Table 4 (continued)

EXEMPT CONCENTRATIONS

Element (atomic number)	Isotope	Column I Gas concentration μCi/ml[1]	Column II Liquid and solid concentration μCi/ml[2]
Gold (79)	Au 196		2×10^{-3}
	Au 198		5×10^{-4}
	Au 199		2×10^{-3}
Hafnium (72)	Hf 181		7×10^{-4}
Hydrogen (1)	H 3	5×10^{-6}	3×10^{-2}
Indium (49)	In 113m		1×10^{-2}
	In 114m		2×10^{-4}
Iodine (53)	I 126	3×10^{-9}	2×10^{-5}
	I 131	3×10^{-9}	2×10^{-5}
	I 132	8×10^{-8}	6×10^{-4}
	I 133	1×10^{-8}	7×10^{-5}
	I 134	2×10^{-7}	1×10^{-3}
Iridium (77)	Ir 190		2×10^{-3}
	Ir 192		4×10^{-4}
	Ir 194		3×10^{-4}
Iron (26)	Fe 55		8×10^{-3}
	Fe 59		6×10^{-4}
Krypton (36)	Kr 85m	1×10^{-6}	
	Kr 85	3×10^{-6}	
Lanthanum (57)	La 140		2×10^{-4}
Lead (82)	Pb 203		4×10^{-3}
Lutetium (71)	Lu 177		1×10^{-3}
Manganese (25)	Mn 52		3×10^{-4}
	Mn 54		1×10^{-3}
	Mn 56		1×10^{-3}
Mercury (80)	Hg 197m		2×10^{-3}
	Hg 197		3×10^{-3}
	Hg 203		2×10^{-4}
Molybdenum (42)	Mo 99		2×10^{-3}
Neodymium (60)	Nd 147		6×10^{-4}
	Nd 149		3×10^{-3}
Nickel (28)	Ni 65		1×10^{-3}
Niobium (Columbium) (41)	Nb 95		1×10^{-3}
	Nb 97		9×10^{-3}
Osmium (76)	Os 185		7×10^{-4}
	Os 191m		3×10^{-2}
	Os 191		2×10^{-3}
	Os 193		6×10^{-4}
Palladium (46)	Pd 103		3×10^{-3}
	Pd 109		9×10^{-4}
Phosphorus (15)	P 32		2×10^{-4}
Platinum (78)	Pt 191		1×10^{-3}
	Pt 193m		1×10^{-2}
	Pt 197m		1×10^{-2}
	Pt 197		1×10^{-3}

Table 4 (continued)
EXEMPT CONCENTRATIONS

Element (atomic number)	Isotope	Column I Gas concentration μCi/ml[1]	Column II Liquid and solid concentration μCi/ml[2]
Potassium (19)	K 42		$3\text{x}10^{-3}$
Praseodymium (59)	Pr 142		$3\text{x}10^{-4}$
	Pr 143		$5\text{x}10^{-4}$
Promethium (61)	Pm 147		$2\text{x}10^{-3}$
	Pm 149		$4\text{x}10^{-4}$
Rhenium (75)	Re 183		$6\text{x}10^{-3}$
	Re 186		$9\text{x}10^{-4}$
	Re 188		$6\text{x}10^{-4}$
Rhodium (45)	Rh 103m		$1\text{x}10^{-1}$
	Rh 105		$1\text{x}10^{-3}$
Rubidium (37)	Rb 86		$7\text{x}10^{-4}$
Ruthenium (44)	Ru 97		$4\text{x}10^{-3}$
	Ru 103		$8\text{x}10^{-4}$
	Ru 105		$1\text{x}10^{-3}$
	Ru 106		$1\text{x}10^{-4}$
Samarium (62)	Sm 153		$8\text{x}10^{-4}$
Scandium (21)	Sc 46		$4\text{x}10^{-4}$
	Sc 47		$9\text{x}10^{-4}$
	Sc 48		$3\text{x}10^{-4}$
Selenium (34)	Se 75		$3\text{x}10^{-3}$
Silicon (14)	Si 31		$9\text{x}10^{-3}$
Silver (47)	Ag 105		$1\text{x}10^{-3}$
	Ag 110m		$3\text{x}10^{-4}$
	Ag 111		$4\text{x}10^{-4}$
Sodium (11)	Na 24		$2\text{x}10^{-3}$
Strontium (38)	Sr 89		$1\text{x}10^{-4}$
	Sr 91		$7\text{x}10^{-4}$
	Sr 92		$7\text{x}10^{-4}$
Sulfur (16)	S 35	$9\text{x}10^{-8}$	$6\text{x}10^{-4}$
Tantalum (73)	Ta 182		$4\text{x}10^{-4}$
Technetium (43)	Tc 96m		$1\text{x}10^{-1}$
	Tc 96		$1\text{x}10^{-3}$
Tellurium (52)	Te 125m		$2\text{x}10^{-3}$
	Te 127m		$6\text{x}10^{-4}$
	Te 127		$3\text{x}10^{-3}$
	Te 129m		$3\text{x}10^{-4}$
	Te 131m		$6\text{x}10^{-4}$
	Te 132		$3\text{x}10^{-4}$
Terbium (65)	Tb 160		$4\text{x}10^{-4}$
Thallium (81)	Tl 200		$4\text{x}10^{-3}$
	Tl 201		$3\text{x}10^{-3}$
	Tl 202		$1\text{x}10^{-3}$
	Tl 204		$1\text{x}10^{-3}$
Thulium (69)	Tm 170		$5\text{x}10^{-4}$
	Tm 171		$5\text{x}10^{-3}$
Tin (50)	Sn 113		$9\text{x}10^{-4}$
	Sn 125		$2\text{x}10^{-4}$

Table 4 (continued)

EXEMPT CONCENTRATIONS

Element (atomic number)	Isotope	Column I Gas concentration µCi/ml[1]	Column II Liquid and solid concentration µCi/ml[2]
Tungsten (Wolfram) (74)	W 181		$4x10^{-3}$
	W 187		$7x10^{-4}$
Vanadium (23)	V 48		$3x10^{-4}$
Xenon (54)	Xe 131m	$4x10^{-4}$	
	Xe 133	$3x10^{-4}$	
	Xe 135	$1x10^{-4}$	$1x10^{-2}$
Ytterbium (70)	Yb 175		$1x10^{-3}$
Yttrium (39)	Y 90		$2x10^{-4}$
	Y 91m		$3x10^{-2}$
	Y 91		$3x10^{-4}$
	Y 92		$6x10^{-4}$
	Y 93		$3x10^{-4}$
Zinc (30)	Zn 65		$1x10^{-3}$
	Zn 69m		$7x10^{-4}$
	Zn 69		$2x10^{-2}$
Zirconium (40)	Zr 95		$6x10^{-4}$
	Zr 97		$2x10^{-4}$
Beta and/or gamma emitting byproduct material not listed above with half-life less than 3 years.		$1x10^{-10}$	$1x10^{-6}$

NOTE a: Exempt concentrations refer to *products* or *materials* containing byproduct materials in concentrations not in excess of those specified in Table 4. Such products or materials may be received, possessed, used, transferred, owned or acquired without registration.

NOTE b: Many radioisotopes disintegrate into isotopes which are also radioactive. In expressing the concentrations in Table 4, the activity stated is that of the parent isotope and takes into account the daughters.

NOTE c: Where a combination of isotopes is involved, the limit for the combination should be derived as follows:

Determine for each isotope in the product the ratio between the concentration present in the product and the exempt concentration established in Table 4 for the specific isotope when not in combination. The sum of such ratio may not exceed "1" (i.e., unity).

Example:

$$\frac{\text{Concentration of Isotope A in Product}}{\text{Exempt concentration of Isotope A}} + \frac{\text{Concentration of Isotope B in Product}}{\text{Exempt concentration of Isotope B}} \leq 1$$

---

[1] Microcuries/milliliter. Values are given only for those materials normally used as gases.

[2] Microcuries/milliliter. Solids measured in microcuries/gram.

Filed with the Secretary of State Sept. 28, 1971 and the Commissioner of Administration Sept. 29, 1971.

INDEX

Reg. MHD

Accelerators 184
Definitions 181
Dental Radiographic Installations 182
Electron Microscope 184
Exemptions 181
Fluoroscopic Units 182
Healing Arts Radium Uses 183
Healing Arts X-Ray Uses 182
Industrial X-Ray Uses 182
Industrial Radium Uses 183
Mobile Diagnostic Units 182
Notification of Incidents and Lost Sources 181
Nuclear Facilities 185
Personnel Monitoring 181
Photofluorographic Installations 182
Prohibition 181

Reg. MHD

Radiation Symbol and Labeling 181
Radiographic Installations 182
Radium Uses 183
Records, Inspections, and Tests 181
Registration Requirements 181
Renewal of Registration 181
Research and Teaching Institutions 184
Safety and Precaution Provision 181
Shielding Provisions 181
Transportation 181
Television Receivers 184
Therapeutic X-Ray Installations 182
Vendor Responsibilities 181
Veterinary Radiographic Installations 182
Violations 181
Waste Disposal of Radium 183
X-Ray Diffraction Units 184

Mr. ROGERS. And, based on these regulations, you then inspect and take action accordingly?

Ms. DOLEZAL. That's correct.

Mr. ROGERS. But you have only found two that are bad; is that right?

Ms. DOLEZAL. The two I had reference to was two times, let's say, per year where we actually close it down. Those are the serious ones.

Mr. ROGERS. You have only had two serious malfunctions?

Ms. DOLEZAL. Where it was necessary to close it down, per year average.

Mr. CARTER. What were those cases, if I might ask, Mr. Chairman?

Ms. DOLEZAL. In one particular case it was not actually something that came directly out of our regulations. It was a case of a temporary location for a particular clinic, and the existing electrical system that was there. However, it was not separated from other parts of the building, so that if somebody used the elevator, the X-ray machine didn't work, and vice-versa kind of thing.

This, of course, could not be tolerated. It would cause a lot of overexposures. So we closed that unit down.

We closed one down because the filtration either had been removed or some other kind of occurrence that it simply was not properly filtered.

Mr. CARTER. You mean the inherent diaphragm——

Ms. DOLEZAL. It was the actual filtration that slips under the collimator; not the inherent, but the added.

Mr. CARTER. Do you have a mechanism for telling when the beam exceeds the size of the film?

Ms. DOLEZAL. Yes, we do.

Mr. CARTER. Do you use that regularly?

Ms. DOLEZAL. Yes, we do, with every survey.

Mr. CARTER. Do you ever have a case of a timer doubling, in clicking off twice and thus giving a double exposure?

Ms. DOLEZAL. We have had that. Actually, the times we have had it is when we had improperly installed certified systems. But yes, we have encountered that.

Mr. CARTER. Have you ever had to force the closure of an X-ray machine? Can you tell us for what reasons?

Ms. DOLEZAL. The two that I had referred to were occasions. Now this was sometime back, we did, because of a timer. This was in a dental office. It was a malfunctioning timer that simply didn't operate properly. The particular practitioner was using a counting procedure, holding the button down rather than a deadman switch stop.

Mr. ROGERS. How many of the X-ray machines do you inspect in your State a year?

Ms. DOLEZAL. Per year; this has varied somewhat because of problems we have with personnel. However, we inspect approximately 200.

Mr. ROGERS. Which is what percentage?

Ms. DOLEZAL. Approximately a third; a third of our X-ray machines. A little over a third.

Mr. ROGERS. So you do a third each year?

Ms. Dolezal. Approximately.

Mr. Rogers. So then you are getting a fairly frequent checking?

Ms. Dolezal. Yes.

In this particular State, we have felt that it would be necessary, desirable, to do busy machines every year—in hospitals—and other machines every 2 years.

Mr. Rogers. Is that your entire State or is that just a region?

Ms. Dolezal. Entire State.

Mr. Rogers. And what is the total number that you have in your State?

Ms. Dolezal. It is a little over 5,600.

Mr. Rogers. 5,600?

Ms. Dolezal. A little over that.

Mr. Rogers. And you do a third, which you said was 200. I am not sure that jibes——

Ms. Dolezal. I am sorry; I meant 2,000, if I said 200.

Mr. Rogers. So you are inspecting 2,000, not 200?

Ms. Dolezal. Yes. I misspoke.

Mr. Rogers. That is all right.

Well, I think that sounds pretty good. That is better than most States, isn't it?

Ms. Dolezal. It is more frequent than many States; that is correct.

Mr. Rogers. But you have only had to correct 2 out of 2,000?

Ms. Dolezal. No, those were the ones we had to close down. There are deficiencies in which we do not close the facility. We review again and again. The frequent inspection has appeared to get better compliance on the part of users.

Mr. Rogers. What about reinspection?

Ms. Dolezal. Since we have a little over 5,600 and we are doing that many each time, they are almost all reinspections.

Mr. Rogers. What about if you have found one out of compliance on the inspection?

Ms. Dolezal. We write the report, which goes to the faculty. They are told of it verbally at the time of the survey. The report requires them to tell us in 30 days how they will correct the deficiency if it has not already been corrected At the end of 30 days, we review what they wrote. If necessary, we will return and resurvey. If they have not responded properly, we resurvey.

Mr. Rogers. It is not an automatic resurvey; it is only if they don't send you a paper that tells what they are doing?

Ms. Dolezal. Right. We would wait the 2 years, or whatever the routine amount would be for that particular facility.

Mr. Rogers. Do you certify all technologists?

Ms. Dolezal. We are in the process of getting certification.

Mr. Rogers. Should that be required federally?

Ms. Dolezal. Some type of certification, indication of training should be required. It may be that Federal guidance with State certification may be the way to go rather than Federal; perhaps. I know in our State we are proceeding and feel we should certify.

Mr. Rogers. What does the conference think?

Ms. Dolezal. The conference simply indicates that certification should be required as an indication of training.

Mr. **Rogers**. They don't say whether it should be State or Federal?

Ms. **Dolezal**. We don't clearly take a stand on it.

Mr. **Rogers**. Do any of your city governments perform inspection functions?

Ms. **Dolezal**. Not in Minnesota.

Mr. **Rogers**. It is all done by the State?

Ms. **Dolezal**. That's correct.

Mr. **Rogers**. What relationship do you have with the city health departments?

Ms. **Dolezal**. You are speaking specifically in the radiation area?

Mr. **Rogers**. Yes.

Ms. **Dolezal**. We have the relation if they have any indication of a problem, they talk immediately with us. If we have any difficulty relating to something or if there is some kind of a known problem, we would get to them. So we have a very definite communication, but they do not inspect.

Mr. **Rogers**. I noticed on page 6 you say:

> Reducing unnecessary exposure may, indeed, save lives, but sampling constraints, data collection limitations and the nature of ionizing radiation exposure effect relationships prohibit the individual States singly or as a group from identifying any specific life that was saved or even predicting the number of lives that were saved by a particular program. We prefer to leave such computation to academia, the Federal Government and others whose resources and interests can best be applied to the study of this nature.

I am not sure of the thrust of that. Do you mean the States should only be concerned in identifying a specific life before action is taken or to see whether a life is affected before action is taken?

Ms. **Dolezal**. No; just the opposite. It is very difficult on these surveys of our 5,600 units to say that, therefore, we have saved so and so, his life, in Minnesota.

Mr. **Rogers**. You can with pelvimetry. You could probably count that up pretty quickly from the research that has been done, I understand. Do you disagree with that?

Ms. **Dolezal**. There is indication that those types of examinations could, indeed, cause leukemias, some malady of the body; that is correct.

Mr. **Rogers**. You could probably count lives quickly there, couldn't you?

Ms. **Dolezal**. If the assumption is made that by preventing this, the life has been saved, that's correct.

Mr. **Rogers**. I am not sure I understand your statement then. Leave it to academia and the Federal Government; you let somebody else worry about that. I am not sure I grasp the thrust of your statement.

Ms. **Dolezal**. The thrust of the statement is basically that as part of our type of program, we are able to perform the function of assisting and reducing the X-ray or the radiation. We do not have the resources whereby we can count this up and, therefore, be able to computate and do the research to say we have saved this many cancers, this many lives.

Mr. **Rogers**. So you don't know what you are doing as far as affecting people's lives. You are just going around and inspecting some equipment, is that what you are telling me?

Ms. DOLEZAL. No, that is not the case. We perform the surveys. We then go to the studies which have been published to be able to relate this and, therefore, we can calculate it.

Mr. ROGERS. Well, I won't pursue that.

Dr. Carter.

Mr. CARTER. Thank you, Mr. Chairman.

What is your training, please, ma'am?

Ms. DOLEZAL. I have a bachelor's degree in math, with a double in physics and academic major also in biology and chemistry and education, and a master's in health physics.

Mr. CARTER. Have you studied radiology?

Ms. DOLEZAL. Yes, that portion.

Mr. CARTER. Ma'am?

Ms. DOLEZAL. That portion that was with health physics.

Mr. CARTER. Do you have a degree in radio technology or anything like that?

Ms. DOLEZAL. Health physics. It is environmental health, with a major in radiation control.

Mr. CARTER. So your job is to go about the State of Minnesota and find dangerous equipment or practices and to stop them, isn't it?

Ms. DOLEZAL. Yes.

Mr. CARTER. And you have told us you do that pretty regularly.

Since you have an enforcement role, would you be able to require all doctors who do pelvimetries to report them to you and then make a statistical analysis of that? Could you require that? You would have to know the persons and follow them, we are told, for at least 20 years to find out if they have bad effects; is that correct?

Ms. DOLEZAL. That is correct. We would have a very difficult time performing that.

Mr. CARTER. Do you think physicians should report on each patient for whom they do a pelvimetry X-ray?

Ms. DOLEZAL. If there is an agency reporting, either Federal or State, if there is an agency that would be able to collect the information and follow through on it.

Mr. CARTER. In other words, if this is a prenatal X-ray, it should be reported; is that your feeling?

Ms. DOLEZAL. It should be indicated.

Mr. CARTER. There is no legislation to that effect, to my knowledge, anywhere. Without such reporting, of course, there would be no statistically reliable way to determine what happens from exposure of fetuses when pelvimetry is done.

Thank you, Mr. Chairman.

Mr. ROGERS. I think those studies have already been done, and we have a projection of what the result is. I think the testimony yesterday gave us that figure.

Mr. CARTER. I am sure they did, but I doubt seriously if they are very accurate. I think many physicians may have hesitated to say the number of pelvimetries they have done, Mr. Chairman.

Mr. ROGERS. So maybe it is worse than we think.

Mr. CARTER. It could be worse, yes, sir.

Mr. ROGERS. It is possible. But the statistics from Washington State, until action was taken, showed that it was pretty bad; the figures they gave us there.

Mr. **Carter.** Beware of the awful avalanche.

Mr. **Rogers.** Beware of the X-ray.

You do not then concern yourself with the types of procedures carried out by the profession with X-ray machines?

Ms. **Dolezal.** Not directly as part of the control program, that is correct.

Mr. **Rogers.** Do they make any reports to you at all?

Ms. **Dolezal.** Of the types of procedures?

Mr. **Rogers.** Yes.

Ms. **Dolezal.** In our survey, our examination, we do find out the types and we get indication of them to compare with normal practice to see if they are within the range of normal practice, but we have no specific statute or regulation on that.

Mr. **Rogers.** But you do gather those statistics?

Ms. **Dolezal.** We do that; that is correct.

Mr. **Rogers.** Thank you so much.

There are some questions we may ask you to answer for the record. We are grateful to you for being here.

Let me just ask you this final question. As I understand, only a limited number of States are members of your association. How many belong to yours?

Ms. **Dolezal.** All.

Mr. **Rogers.** All do. I misunderstood.

Ms. **Dolezal.** All the States belong.

Mr. **Rogers.** Everyone has joined the conference?

Ms. **Dolezal.** That is correct.

Mr. **Rogers.** Good.

Thank you so much. We are grateful to you for your being here today.

Ms. **Dolezal.** Thank you.

Mr. **Rogers.** Now on behalf of the American Dental Association, we have Dr. Robert Goepp, who is a member of the American Dental Association's Council on Dental Research and head of the section of oral pathology and radiology, professor of oral pathology, Zoller Clinic, University of Chicago; Dr. John Stanford, who is secretary of the Council on Dental Materials and Devices, American Dental Association.

We welcome you to the committee. Your statements will be made a part of the record in full at this point.

We express our appreciation for your being here. You may proceed as you desire.

STATEMENT OF ROBERT GOEPP, D.D.S., MEMBER, COUNCIL ON DENTAL RESEARCH, AMERICAN DENTAL ASSOCIATION, ACCOMPANIED BY JOHN STANFORD, D.D.S., SECRETARY, COUNCIL ON DENTAL MATERIALS AND DEVICES

Dr. **Goepp.** Mr. Chairman, Congressman Carter, Congressman Ottinger, my name is Dr. Robert A. Goepp from Chicago, Ill. I am appearing today on behalf of the American Dental Association. I am professor of oral pathology and head of the section of oral pathology and radiology of the Zoller Clinic of the University of Chicago.

I am also the acting director of the Zoller Clinic. I am also both a consultant in radiology to the association's Council on Dental Materials and Devices and a member of its Council on Dental Research.

I am accompanied by Dr. John Stanford, the secretary of the Council on Dental Materials and Devices.

For the sake of economy of time, we have a prepared statement which is available to you, and I would prefer to read only some selected highlights. [See p. 626.]

Mr. ROGERS. That would be helpful to the committee.

Dr. GOEPP. Which would perhaps lead to questions.

Mr. ROGERS. Certainly.

Dr. GOEPP. We share this subcommittee's concern about unnecessary use of X-rays and we welcome the opportunity to present our views. Additionally, we have addressed certain specific issues such as low-level radiation effects, such as the status of dental radiology teaching issues which have been raised.

We have addressed these in a separate document which we have submitted to you.

Mr. ROGERS. It will be made part of the record, without objection.

[The document referred to was not available to the subcommittee at the time of printing.]

Dr. GOEPP. One of the important issues is concerning dental education. For example, the typical dental student receives directly 70 hours of instruction on radiology. The hygienist, a dental ancillary, receives 55 hours. The student receives supplemental instruction in such related instructional areas as oral diagnosis treatment planning. In other words, the use of radiology sort of transcends many aspects of dentistry, and they are not formally identified in dental education as an experience in radiology, but radiology is used.

These courses in training, of course, are tested in the form of the national board examinations and State board examinations which lead to licensure. Ninety-eight percent of all eligible students take the national examinations. For example, a review of their performance on this examination is a reflection of the development of their knowledge.

But, there is a need for encouragement, and there is a need for support in the implementation of improvements in radiologic practice previously recommended by the American Dental Association and other interested agencies. Such encouragement and support should be directed to some dental schools, some clinical settings and some policies of health care funding systems, including public welfare programs.

The exposure of living tissue to ionizing radiation produces biological effects varying in degree according to the type of and amount of radiation exposure and the kind of tissue exposed.

As mentioned earlier, we have gone into detail in particular on the interesting subject of low-level exposure. As practitioners of the healing art, the dentists of the Nation have a primary responsibility to protect and improve the health of our people and to insure that everything done in the dental office is directed precisely to protect the patient. The control of excessive radiation, that is, the use of radiation beyond that required for the individual patient, is a major concern of dentistry.

On the other hand, it would be impossible to maintain dental practice at the level that American people rightfully expect without the use of diagnostic X-rays in dentistry. Thus, we have a dual rôle to recognize at the same time that X-rays must be employed with the most scrupulous care in order to serve our patients efficiently.

While there have been many activities on the part of the American Dental Association and on the part of other interested agencies, we could cite one here.

For example, the American Dental Association, along with the Public Health Service, have distributed to health agencies at the State level over 100,000 filters to improve the quality of diagnostic dental X-ray beams and over 100,000 collimators to restrict the size of diagnostic dental X-ray beams.

These combined efforts of the Association and the Public Health Service have resulted in an almost universal meeting of dental X-ray units in the United States, for the minimum requirements for filtration and collimation. These are only two of such activities which have been undertaken.

The American Dental Association has long recommended that the use of X-radiation for diagnostic purposes should be made only after careful consideration of both the dental and general health needs of the patient. The deciding factor is, of course, the total welfare of the patient.

The nature and extent of diagnosis required for patient care can constitute the only rational basis for determining the need or frequency of dental radiographic examination. The Council of the American Dental Association does not agree with the routine requirement of post-operative radiographs to show proof of service rendered. The issue of substantiation of claim, in effect, X-raying for bookkeeping purposes, is considered in more detail, again, in our additional statement.

The number of exposures to be made in examination of the patient should be based on the patient's history, findings in the head and neck area, and all this information should be put together in order to make a sound clinical decision as to what is best for the patient.

We thank you for the opportunity to make this abbreviated statement on behalf of the American Dental Association.

As I said earlier, copies of this entire statement and additional information of course have been submitted to your committee.

Thank you, sir.

[Dr. Goepp's prepared statement follows:]

STATEMENT OF
THE AMERICAN DENTAL ASSOCIATION
BEFORE
THE SUBCOMMITTEE ON HEALTH AND THE ENVIRONMENT
COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE
UNITED STATES HOUSE OF REPRESENTATIVES
JULY 13, 1978

Mr. Chairman and Members of the Subcommittee:

My name is Dr. Robert Goepp from Chicago, Illinois. I am appearing today on behalf of the American Dental Association. I am Professor of Oral Pathology and Head of the Section of Oral Pathology and Radiology of the Zoller Clinic, University of Chicago. I am also both a consultant in radiology to the Association's Council on Dental Materials and Devices and a member of its Council on Dental Research. I am accompanied by Dr. John Stanford, Secretary of the Council on Dental Materials and Devices.

We share this subcommittee's concern about unnecessary use of x-rays and welcome the opportunity to present the views and activities of the American Dental Association on the safe and effective use of x-rays in dentistry.

Mr. Chairman, the ADA received your invitation to testify and prepared a statement before receiving your specific questions. In response to those questions we have prepared a statement for the record. But we also believe we need to reply to certain questions that have been raised in testimony before this subcommittee, specifically questions about dental x-rays and the education and training of dental students in administering and interpreting x-rays. Previous witnesses have criticized the dental profession for supposedly failing to educate itself to the possible health risks of exposure to unnecessary radiation. Quite the contrary is the case. The typical dental student receives, directly, 70 hours of instruction on radiology; the hygienist receives 55 hours. The dental student receives supplemental instruction in such related instructional areas as oral diagnosis and treatment planning. The national board examinations for dentists and dental hygienists have an extensive series of questions testing -- before licensure -- the knowledge the graduating student has acquired with regard to radiology and radiation protection. Ninety-eight percent of eligible students take this examination. This is their national board examination. We do not believe federal legislation is required in this regard.

The exposure of living tissue to ionizing radiation produces biologic effects varying in degree according to the type and amount of the radiation exposure and the kind of tissue exposed. Any consideration of x-rays in dentistry must necessarily balance these health risks with health benefits. That x-radiation is a useful, valuable and necessary diagnostic and treatment tool is unquestioned.

Radiation thrift is, therefore, the keynote of such considerations, always balancing the possible biologic hazard or risk against the benefits anticipated through the acceptance of additional radiation exposure, and always keeping to an absolute minimum the exposure levels utilized in deriving these benefits To cite but two benefits, the diagnostic contribution of radiography in the effective management of dental caries and the conspicuous benefits accruing from the use of radium or x-rays in cancer therapy are convincing examples. There is, therefore, cause enough to consider that some deliberate exposure to ionizing radiation may be deemed desirable or justifiable. The question, then, is in what circumstances and under what conditions of use this may be prudently recommended and undertaken in the course of our professional activities.

The American Dental Association, in cooperation with such organizations as the National Council for Radiation Protection and Measurements, the American National Standards Institute, the American College of Radiology and the American Academy of Dental Radiology, supports activities for effective radiation protection for the dentist, for his office personnel, for his patients and for the public at large. And since in the final analysis the responsibility for implementing radiological health practices and procedures rests with the individual dentist, the Association has for many years vigorously supported programs of information and education in these matters, both through its own agencies and in cooperation with similar programs of governmental agencies at national, state and local levels. All of these efforts have been designed to emphasize that the use of x-radiation for diagnostic purposes should be kept to a minimum, always justifiable on an individual basis in terms of a prudent balance between the expected yield of diagnostic information and the element of biologic risk entailed.

As practitioners of a healing art, the dentists of the Nation have a prime responsibility to protect and improve the health of our people and to insure that everything done in the dental office is directed precisely to this end. The control of excessive radiation - that is radiation beyond the needs of the individual patient - is a major concern of dentistry, as, I am sure, it is with the members of this subcommittee.

Over the years, and particularly in the past three decades, there has been an immense improvement and expansion of the dentist's resources, enabling him to render his patients an ever higher quality of care. X-rays are an essential component of the modern dental practice, an indispensable adjunct to the diagnosis of many diseases of the mouth and of the bones of the face and jaw.

Approximately two-thirds of a tooth is below the surface of the gums, and pathological conditions existing in relation to the tooth root cannot be noted by clinical observation. Bone changes in the jaw cannot be observed by means other than the x-ray film until they have increased to such a size as to produce gross deformities or obvious systemic reactions.

Diseases of the supporting structures of the teeth can be observed in their incipient stages only by use of x-ray film. The presence or absence of anomalies in children's mouths can often be determined with x-rays and remedied at an early age.

The x-ray film is used, as well, as an integral part of dental therapy. For example, the practice of endodontics, the specialty of sterilizing and treating the root canals in nonvital teeth, is totally dependent upon the x-ray film in order to "see" the root end of the involved tooth so that it may be treated properly.

As a postoperative measure, x-ray films are necessary for such purposes as determining the degree of bone healing and the replacement of pathologic areas with normal tissue.

It is not too much to say, then, that it would be impossible to maintain a dental practice at the level the American people rightfully expect without x-rays.

At the same time, the dentist fully recognizes that x-rays must be employed with the most scrupulous care. As with many of the drugs and instruments used in a dental practice, misuse of x-rays can have harmful consequences.

The Association's overall activities have concentrated on five methods of limiting the radiation exposure of the patient, as well as protecting the dentist and his office personnel.

These are -

(1) Limitation of x-ray beam size to that required to expose the film;

(2) Insertion of metal filters to remove unnecessary radiation from the x-ray beam;

(3) Use of higher kilovoltage;

(4) Use of higher speed or more sensitive x-ray film; and

(5) Limitation, as mentioned, of the frequency and extent of radiation examination consistent with good practice.

For example, Association activities in the foregoing areas in cooperation with the Public Health Service resulted in distribution to all health agencies of over 100,000 filters and almost 100,000 collimators or beam limitors for installation in dental x-ray machines manufactured before August 1, 1974. This combined with the federal standard for diagnostic x-ray systems and the Association's standard for x-ray machines, mentioned at a later point, have resulted in almost 100 percent of the dental units in the United States meeting or exceeding the minimum requirements for filtration and collimation. These two factors are primary to reduction of unnecessary radiation to the patient.

The Association has developed standards for diagnostic dental x-ray equipment and dental x-ray film along with guidelines for safe and effective accessory devices for x-ray machines and rapid processing devices for dental x-ray film.

When a standard for x-ray film (American National Standards Institute/American Dental Association Specification No. 22) was adopted in 1969 manufacturers stopped making the slower speed films that had contributed in the past to unnecessary radiation exposure. A pending revision of that standard will omit the medium speed film (ANSI Group C) and will cover only very high speed products, thus reducing even more the patient's exposure time. According to surveys conducted by the Association more than 90 percent of the dentists now use the high speed film.

The standard for dental x-ray equipment (American National Standards Institute/American Dental Association Specification

No. 26) adopted in 1974 was formulated with the assistance and participation of many interests including the Bureau of Radiological Health of the Federal Food and Drug Administration. The information and data obtained during the formulation of that standard was used by the FDA in the development of federal regulations and performance standards for diagnostic x-ray systems. The standard requires that the equipment be properly filtered to remove soft x-rays which only expose the patient to unnecessary radiation and do not produce dental radiographs. Beam limitation is also provided by the standard to reduce tissue exposure. Most dental x-ray equipment is designed with circular beam limitation. The Association also has formulated guidelines for use in its Acceptance Program for accessory devices for x-ray machines that will further restrict the beam to the shape of the film. Those guidelines provide for a proper alignment and restriction of beam as well as providing means to eliminate scattered x-rays originating behind the outer end of the cone.

Guidelines for accepting rapid processing devices for x-ray film have also been formulated by the Association. Such devices provide for the handling of very light sensitive high speed films without resorting to the conventional darkroom. The automated system reduces errors and necessity to remake films which cause unnecessary radiation to the patient.

The standards and guidelines are used to govern submissions by industry to the Association's Council on Dental Materials and Devices under its Certification and Acceptance Programs. By these programs the Council establishes, after appropriate evaluations, lists of recommended products which are used by the dentist in selection of safe and effective materials and units. The Council's programs provide that products in dental radiology must be accepted prior to being eligible to advertise or exhibit through Association media.

In addition to technological improvements and development of standards to improve equipment and make it safer, the Association has continued its educational program to provide the dentist and his auxiliary what they need to know about efficient techniques of operation.

The American Dental Association has consistently stated that the use of x-radiation for diagnostic purposes should be made only after careful consideration of both the dental and the general health needs of the patient. The deciding factor is the total welfare of the patient. The nature and extent of diagnosis for required patient care constitute the only rational basis for determining the need or the frequency of dental radiographic examination. The Council does not agree with a routine requirement of post-operative radiographs to show proof of service rendered. In other words, diagnostic radiography should be limited to those instances in which the dentist anticipates that the information he is likely to obtain will contribute materially to proper diagnosis, treatment, or prevention of disease, or all of these. The number of exposures to be made in the examination and the history of the patient's radiation exposure, especially to the head and neck, should be considered in making such an evaluation.

Thank you for the opportunity to make a statement on behalf of the American Dental Association. Copies of Association standards and Council programs are available for the record if the Subcommittee desires. We will be happy to try and answer any questions.

Mr. ROGERS. Thank you very much, Dr. Goepp.

Dr. Carter.

Mr. CARTER. Thank you, Mr. Chairman.

When you give a dental examination, Dr. Goepp, do you usually do a full mouth X-ray of those patients or not?

Dr. GOEPP. Probably not. I would say with the qualification that we usually do what is indicated, and that is based in whatever the patient's problem is.

Now, if we cast a patient in the light of being an unknown patient of which we know nothing and that there is a full dentition and there is a moderate incidence of the usual dental disease, such as caries and peridontal disease, it is most likely that a full mouth examination is the best way to gain the needed information about the patient.

Mr. CARTER. How many millirads does it take to do a full mouth dental X-ray examination?

Dr. GOEPP. These amounts have been measured, sir, but one is hesitant to put numerical values on these things without qualifying such. We must realize some areas are overlapped in exposure. Other areas are exposed perhaps only once or twice. Since all this material must be integrated, the numerical value may mean little if we apply, for example, 800 millirads to the facial skin or the facial area, we would not expect too many consequences.

On the other hand, 800 millirads to a nearby area, such as the thyroid, might have a far more profound effect on the patient's welfare.

Mr. CARTER. Do you have many apical abscesses which are nonsymptomatic?

Dr. GOEPP. How many?

Mr. CARTER. Do you have many apical abscesses which are nonsymptomatic?

Dr. GOEPP. Yes, this is possible. However, what you have described is probably the classic dental toothache, with the swollen jaw and the acute distress.

Mr. CARTER. What I am describing is one in which you have minimal infection but which can be seen by an absence of tissue, I believe, in the area of apex.

Dr. GOEPP. You mean in an X-ray examination?

Mr. CARTER. Yes.

Dr. GOEPP. It is true in dentistry, we encounter a great deal of silent disease; disease that does not give much outward, if any, sign. And we do discover the silent diseases on X-ray examination.

Mr. CARTER. There have been cases of bacterial endodontics causes by these.

Dr. GOEPP. It is true. And it is important to realize while most people think of dental disease or the consequences of dental disease merely as a disability, the loss of a structure, it should be pointed out that the case you describe is a case where dental disease can result in fatality, and it does happen.

Mr. CARTER. You have 70 hours training per student?

Dr. GOEPP. Yes, sir.

Mr. CARTER. Is that training usually with an instructor?

Dr. GOEPP. Yes.

Mr. CARTER. For a small number of students, is that correct?

Dr. GOEPP. Yes. In the dental education scene there is both one-to-one instruction because of the nature of the thing being taught, and then there is group instruction, and this will vary in small groups to perhaps entire class sizes for lecture.

Mr. CARTER. Together, the instructing dentist and dental student perform the X-rays as a usual thing; is that correct?

Dr. GOEPP. Yes. In an apprentice-type like relationship, yes, sir.

Mr. CARTER. Of the 70 hours total how many hours each day are involved in this teaching and learning process?

Dr. GOEPP. The 70 hours, of course, are the formal exposure. I did allude earlier to the informal exposure, and that is a student treating a patient in the clinic may have need for an X-ray examination to follow the course of a treatment or to explore new findings that have occurred in the patient. He will undertake to take the patient to the radiology clinic and request such an examination; and then here we have the informal act of the apprenticeship learning with the teacher to conduct this examination.

There is no good way, really, unless we went over every patient's chart, to see what time was spent on radiology. There is no good way to measure how many hours that involves.

Mr. CARTER. Yes, sir. But in formal teaching, you have 70 hours. Is that just about an hour or so a day or do you have more hours?

Dr. GOEPP. These courses are usually not scheduled on a daily basis, sir, but they may be 2 hours or 4 hours on 1 day of the week.

Mr. CARTER. That is what I had understood. Actually, since ionizing radiation may cause difficulty, are you in the Association and in your relationship with other dentists mindful of the need to tell them the danger of radiation exposure? Are you informing them of this so they may take care not to give unnecessary X-rays?

Dr. GOEPP. Yes, sir, we have several vehicles through which to do this. The first and most constant vehicle is the monthly publication of the American Dental Association Journal. In this journal there are reports of specific activities. In one of the current reports is an issue dealing with radiation safety, and these are so pointed out.

In addition, the Association sponsors scientific meetings, participates in scientific meetings and, again, this particular council of the American Dental Association constantly promotes and promulgates knowledge about radiation protection, use of radiation, so forth.

However, one must realize that the Association cannot dictate to each individual practitioner in our society. The responsibility rests with the doctor who has his hand on the patient, and we have to defer to his decision on what he wants to do. He cannot be told what to do.

Mr. CARTER. I have one more question at this time, and I may have a few more later, Mr. Chairman.

Has an acceptable method been developed for determining the whole body equivalents of dental X-rays?

Dr. GOEPP. This is, again——

Mr. CARTER. In other words, what is the effect of a dental X-ray of 500 millirads on the whole body?

Dr. GOEPP. By whole body equivalents, do you mean the whole body exposure?

Mr. CARTER. Yes, sir.

Dr. GOEPP. Yes, sir, this has been measured many times because of the changes in the state of the art, let's say, of radiation protection. If we look at studies from 20 years ago, exposure to such important tissues were detectible, and although in actual numerical amounts rather low, they were relatively high compared to what one should receive.

Periodically these things have been measured in the last 20 to 25 years, and there has been a distinct reduction.

Mr. CARTER. Are you careful not to irradiate the gonads?

Dr. GOEPP. Yes, we certainly are. And one might think this is somewhat humorous, but in older dental textbooks of several decades ago, there are examples of how to do certain examinations which, for ease and lack of equipment, say, put the film on a table and have the patient bend over to get the certain part of their anatomy, without realizing underneath the table were gonads, and unless the table was made of lead, this is not a good idea. We also advocate the use of lead aprons in order to protect the gonads.

This sort of thing has totally disappeared from the educational literature.

Mr. CARTER. Are your radiographics principally of the cone type?

Dr. GOEPP. Again in conducting the ordinary dental examinations where the small films are placed inside of the mouth, these cones are extraordinarily useful. In fact, the examination would be an adventure without them. These cones tell us how large the beam is going to be, they tell us the right distance from the machine to the patient's skin. Inside the cone, of course, are incorporated the collimators and filtration parts to characterize the beam, to make the beam a certain quality that we want, to restrict the beam to where we want it to be.

Mr. CARTER. Thank you very kindly.

Mr. ROGERS. Mr. Ottinger.

Mr. OTTINGER. I have no questions.

Thank you, Mr. Chairman.

Mr. ROGERS. How many radiologists do you have on the staff of the American Dental Association? Any?

Dr. GOEPP. Perhaps Dr. Stanford could respond to that.

Mr. ROGERS. Certainly.

Dr. STANFORD. Those who would be qualified 100 percent as a radiologist, there would not be any, Mr. Rogers. However, there are several, one gentleman in the research institute who has training in radiology who is doing research with the inter-oral source radiographic equipment.

There is the present editor, actually, of the Association who has a specialty in pathology and has a background in radiobiology, and then there is also one of the assistant executive directors of the Association for Scientific Affairs who is an oral pathologist also in the areas of recognizing effect of radiation as far as dentistry is concerned.

So that while we may not have specifically on the staff of my Council a radiologist, we have access to those gentlemen with the training to assist us. The Council also has seven consultants in radiology appointed by the Association's Board of Trustees to assist us. The American Academy of Dental Radiology also provides assistance.

[The following information was received for the record:]

AMERICAN DENTAL ASSOCIATION
211 EAST CHICAGO AVENUE CHICAGO ILLINOIS 60611 • AREA CODE 312 440-2500
440-2508

August 8, 1978

Mr. Paul G. Rogers, Chairman
Subcommittee on Health and the Environment
Committee on Interstate and Foreign Commerce
U.S. House of Representatives
Room 2125, Rayburn House Office Building
Washington, D.C. 20515

Dear Mr. Rogers:

I want to first express my appreciation as well as that of Dr. Robert Goepp for the opportunity to present activities of the American Dental Association related to the use of radiation in dentistry before your Subcommittee on July 13, 1978. Responses which hopefully will acknowledge the questions posed during the hearings are enclosed. In addition to the material submitted I would like to make the following comments:

> As I indicated there are no radiologists per se on the staff of the Council on Dental Materials and Devices of the Association however the following are official consultants to the Council in the area of radiology and we frequently call upon them for advice. These consultants are officially appointed by the Board of Trustees of the Association.
>
> a. Dr. Ray W. Alcox, Head of Radiology, University of Nebraska, School of Dentistry
>
> b. Dr. Robert A. Goepp, Acting Director of Zoller Clinic, University of Chicago and a member of National Council on Radiation Protection and Measurements
>
> c. Dr. Lincoln R. Manson-Hing, Head of Radiology, University of Alabama, School of Dentistry

d. Dr. Alan Reiskin, University of Connecticut, School of Dentistry

e. Prof. Albert G. Richards, Head of Radiology, University of Michigan, School of Dentistry

f. Dr. Donald T. Waggener, University of Nebraska, School of Dentistry

g. Dr. Robert J. Nelsen, Rockville, Maryland, a member of National Council on Radiation Protection and Measurements

The Council also maintains liaison with the American Academy of Dental Radiology which has appointed the following committee to give advice to the Council.

a. Dr. S. Julian Gibbs, Vanderbilt University, Department of Radiology

b. Dr. Gus C. Pappas, Ohio State University, School of Dentistry

c. Dr. William K. Collett, University of Florida, School of Dentistry

d. Dr. James Miller, Bureau of Radiological Health, Food and Drug Administration

The Council therefore does have input from the radiological area in its decisions and recommendations.

Additional supplemental information on the Associations' activities and the responses to other questions from your committee were filed with you on July 13, 1978.

If you should have any questions I will be happy to respond further.

Sincerely yours,

John W. Stanford

John W. Stanford, Ph.D.
Secretary
Council on Dental
Materials and Devices

JWS:sam
Enclosures
cc: Dr. C. Gordon Watson
Dr. Richard W. Tiecke
Dr. John M. Coady
Mr. Hal M. Christensen
Mr. Bernard J. Conway
Dr. Robert A. Goepp
Mr. W.E. Williamson

Mr. **Rogers**. Pathologists?

Dr. **Stanford**. They are pathologists, yes, sir.

Mr. **Rogers**. You indicate you are funding some research; is that correct, on dental radiology?

Dr. **Stanford**. Yes, sir. Within the Research Institute of the American Dental Association Health Foundation there are projects going on; one of these dealing with the modification and development improvement of an X-ray device which is that whether the source of X-rays is intraoral.

There have been some of these pieces of equipment on the market in prior years, but because of problems of shielding and other problems, they are not used as widely as they were. But these devices have been worked with the research that is showing at the present time an improvement in image quality, less distortion of the radiograph, and there are other benefits.

There are also some disadvantages that have to be overcome, and those deal with the actual use of the device itself as far as technique is concerned.

Mr. **Rogers**. How much money is being spent on research in radiology, dental radiology?

Dr. **Stanford**. That is difficult to say, sir, because——

Mr. **Rogers**. Would you let us know for the record? I realize you may not have it.

Dr. **Stanford**. I will be happy to.

May I qualify it, Mr. Rogers, in that the research that is going on with the association, part of that will be paid for by direct dues from the association members and then part of it is by Public Health Service grants.

Mr. **Rogers**. That is all right. Just so you can let us know what you are putting in either from dues or the ADA itself and what project. We don't object to mixing of the funds. I wanted to know for the record what is being done, what are the projects, your principal investigator. If you could give that for the record.

Dr. **Stanford**. I will be happy to do it.

[The following information was received for the record:]

PAST AND CURRENT PROJECTS WITH COSTS INVOLVED

There are several past and current projects in radiology carried out in the Research Institute of the American Dental Association Health Foundation and in the laboratories of the Council on Dental Materials and Devices. The projects follow with approximate direct costs involved. No estimate of indirect costs is made:

1. Radiation dose and image quality for radiographic holding, aligning and shielding accessories, 1973, $32,100.
2. Intraoral source radiography, 1975, $12,064, contract with Bureau of Radiological Health. For same project since 1973 the Association has contributed from membership dues a total of $150,000. 1978 - $25,000. Dr. C.M. Schoenfeld, ADAHF Research Institute is principal investigator.
3. X-ray equipment, revision of existing standard ANSI/ADA Specification No. 26, 1978 - $15,000, Council on Dental Materials and Devices project.
4. X-ray film, revision of ANSI/ADA Specification No. 22, 1978 - $18,000, Council on Dental Materials and Devices project.
5. Evaluation programs for x-ray films, accessory devices to x-ray machines to limit beam size and shape and automatic film processors, 1978 - $5,000, Council on Dental Materials and Devices project.

A brief review of projects being conducted in the Research Institute follows:

Radiological Studies: Automatic and manual processing of both screen and non-screen radiographic films were studied, and comparisons were made of spatial resolution, sensitometric analysis, and optic density variations in the presence of uniform exposure. Resolution was essentially unaffected by the means of processing; however, a typical automatic technique required about 30% higher radiation exposure than a typical manual technique. An increase in processing temperature appears to be a more effective means than an increase in processing time to reduce the amount of additional exposure required for automatic processing. On the other hand, an increase in processing temperature would undoubtedly accelerate the time dependent degradation of processing solutions. This study is part of a program to optimize the quality of dental films while reducing the level of radiation used to obtain the films. These results should be considered preliminary, since it did not emcompass many possible variables.

A study to measure the image quality obtainable by three basic radiographic techniques was also carried out. The radiographic techniques included in the study were: periapical and bitewing radiography, curved surface tomography and intraoral source radiography. Image quality was measured only in terms of resolution. Measurements were made in a spatial frequency range that corresponds to the scale from gross anatomical detail to the limits of resolution of the human eye. The analysis of resolution was a measure of the performance of the complete radiographic systems including the effect of: the focal spot, the geometry of projection, and the image receptor. The experiments were designed to characterize each radiographic system by use of a set of variables that could presently be considered typical of each technique. Also, the dependency of resolution on spatial orientation and the responsiveness to changes in image receptor speed was measured for each technique. In general, the results reinforced interest in the potential merits of intraoral source radiography in optimizing the quality of dental films while reducing the level of radiation used.

A program of collaboration with manufacturers of rod anode x-ray generators has continued. The goal of the program is to develop optimum x-ray units for intraoral source radiography. The collaboration is converging upon submissions to the Bureau of Radiological Health and upon the initiation of clinical applications of the intraoral source technique.

It is believed that the Committee should know that a number of grant applications to the National Institute of Health have been approved by reviewing bodies but not funded due to inadequate funds or higher priorities in other program areas.

Mr. ROGERS. Dr. Allen Reiskin informed the subcomittee—perhaps you heard him yesterday—that a survey by Pennsylvania Blue Shield found two-thirds of the preauthorization dental X-ray submitted to Blue Shield to be inadequate as a basis for determining the efficacy of the proposed dental treatment.

Furthermore, one half to three-fourths of the films were technically unsatisfactory. Would you think that would be generally true?

Dr. GOEPP. There are many ways one can look at situations like this, and I would rather speak from my own experience.

It is disappointing to even see one technically incompetent film. Nonetheless, these things do happen because as human beings, we are fallible.

Mr. ROGERS. Half, two-thirds is a pretty frightening figure.

Dr. GOEPP. This is a large number, of course. We must remember included in these numbers are films that cannot be done any better. In our type of clinic we see many patients that are not muscularly able to cooperate; we are happy to get a film. And it does not meet ideal diagnostic standards.

By the way, this is also a point that has been raised by some thoughtful dental radiologists that this pursuit of ideal standards by which these studies were measured are perhaps not really well thought out and are not really realistic. One could ask himself, my God, if three-quarters of the dental films are no good, how come we are not all much sicker than we are?

Mr. ROGERS. Maybe we haven't had 10 to 20 years yet since our X-rays. I don't know that answer yet.

Have you had an opportunity to look at this study?

Dr. GOEPP. I saw that. That is a rather old study. I saw that 8 or 10 years ago.

Mr. ROGERS. Has it been refuted by any other study?

Dr. GOEPP. I don't think that area has been very well studied.

For example, we point out in our ancillary document that there is a serious unnecessary exposure risk associated with the sort of thing you are talking about.

Mr. ROGERS. What can we do to improve that situation, do you think, and what does the ADA suggest doing?

Dr. GOEPP. There are a number of things that can be done, and we could ask you for some help in finding——

Mr. ROGERS. This is what we need to know.

Dr. GOEPP. In finding ways to implement what are already good rules and regulations and also for some help in improving the quality of dental radiology teaching. We describe this, again, in detail in the additional document.

Mr. ROGERS. We have given captation awards to schools of dentistry to improve and upgrade the quality of dental education. Evidently we still have much to accomplish in the radiological fields and I think probably, too, we are learning more about the effects of radiology and that is bringing more emphasis to the problem, I presume?

Dr. GOEPP. Yes, sir, you are right.

Mr. ROGERS. We also have been informed that 90 percent of the dental X-rays in Connecticut, for instance, are performed by dental assistants with no formal radiological training. Would that be typical of the country nationwide?

Dr. GOEPP. There have been a number of studies which have tried to generate information like that; 90 percent, again, is an attention-getting number, and one wonders how accurate it might be. However, the real issue is this: That it is possible for an untrained person to conduct an X-ray examination. The ADA has fostered the conducting of X-ray examinations by people trained in this matter which range, of course, from the dentist to the dental hygienist, and the dental assistant. There are courses available at meetings, so forth, to renew the basic knowledge these people received in their fundamental training.

Mr. ROGERS. Do you support the certification or licensing of technologists?

Dr. GOEPP. There is presently a timely issue in the Federal Register which might be useful in answering that question. Right now the Federal Register has published about positive beam limitation devices.

This applies overwhelmingly, of course, to medical radiology, and it is directed to the subject of making the beam the size of the film, which is a technologist's responsibility. Every technologist, of course, should know how to do that and should accomplish that task.

If the Federal Register is placing so much emphasis on automatic beam limiting devices, then there must be a problem there. These people in medical radiology are licensed and registered. Apparently the licensing and registration did not accomplish what was intended.

Mr. ROGERS. This concludes 30 percent of the dental X-rays were taken by dental assistants with no radiological training. So I presume they are not licensed nor certified?

Dr. GOEPP. That's right. There is no mechanism for certification or licensure

Mr. ROGERS. What I am asking is, should there be?

Dr. GOEPP. Yes.

Mr. ROGERS. Does ADA support that?

Dr. GOEPP. No.

Mr. ROGERS. Why not.

Dr. GOEPP. No; for the reason I just pointed out; that medical technologists are licensed and have been licensed for a long time, and yet great attention is being paid to automating some procedure that they are all supposed to be able to do and they don't do.

Now the question here, I think, at least my answer would be that the issue is one of education rather than licensure. Many evils can be hidden behind licensure. Licensure sometimes supplies false security. We presume the person knows what he is doing.

Mr. ROGERS. I am not sure we can get all these people to go back to school. But a quick licensure procedure could require immediately a certification and qualification. I am not sure I follow your reasoning exactly; otherwise, I am not sure we would even have to have licenses or qualifications for dentists. I don't think you would put us in that position.

Now let me ask this—I won't pursue that. I think any suggestions you have as to how we can correct these deficiencies would be helpful. Also, if you could comment to some degree on the figures of two-thirds and three-fourths on the actual X-rays taken that are not sufficient.

How many of the instructors in the dental schools who are instructing students in the use of X-ray are radiologists themselves?

Dr. GOEPP. Very few. In fact, there are only a handful of people in the entire country who are really knowledgeable to, let's say, the fullest possible degree today in dental radiology. There are only a handful.

Mr. ROGERS. Should that be changed; should that be corrected?

Dr. GOEPP. Yes; I would think so. And I would advise, or I would ask if we could have such help. It would be appreciated.

Mr. ROGERS. In other words, we really ought to have radiologists teaching that in our schools; I presume medical as well as dental?

Dr. GOEPP. Yes.

Mr. ROGERS. And ADA would support that?

Dr. GOEPP. I presume so. We cannot speak for the Association.

Mr. ROGERS. Excuse me?

Dr. GOEPP. We cannot speak for the association as a matter of policy. We have put that forth in the beginning of our statement.

Mr. ROGERS. I thought you were testifying for the ADA.

Maybe I misunderstood.

Dr. STANFORD. Mr. Chairman, I think what Dr. Goepp said was in response to the questions that came to us. We have responded as our opinions and the opinions of the association or the council where official actions have been taken.

With respect to the question you are asking now, sir, it is in the area of education and training, and this is the reason Dr. Goepp was making the statement that what we are saying would be our opinions because we are not in the area of education. We are in the area of materials, equipment and research and that we would be happy to get you any opinion or so, in that particular area, if you would so desire.

Mr. ROGERS. Is there anybody here who would know?

Dr. STANFORD. No, sir, I do not believe we would have anyone present who could answer that question.

[The following information was received for the record:]

The association has no policy regarding the necessity of an instructor of dental radiology being a radiologist. The instructor however should have expertise in the diseases of the mouth and should understand the health effects of radiation as used in dentistry.

Mr. ROGERS. If you would get us the opinion of your people for the record, it would be helpful.

Earlier testimony also revealed that in practice, American dental schools teach dental students to use X-rays as a routine screening procedure and, apparently, most of the schools, if not all, require X-ray exams of all patients prior to any treatment; is that correct?

Dr. GOEPP. That is true for some schools, sir. It is not true for all schools.

Mr. ROGERS. How many would you think? Could you give any rough estimate?

Dr. GOEPP. I have personal experience with perhaps four or five schools; I have seen four or five that require routine X-ray examination.

Mr. ROGERS. Would you let us know for the record?

Dr. GOEPP. We certainly can get that information.

[The following information was received for the record:]

ROUTINE FULL MOUTH RADIOGRAPHIC EXAMINATIONS

A review of information available to the association at present makes it impossible to specifically state the number of schools that require routine full mouth radiographic examinations of patients in school clinics. It is estimated that the numbers would be high since many of the patients who come to dental school clinics are from the lower income group and have not had recent dental examinations. A full mouth radiographic examination therefore would be and should be a part of the diagnostic treatment program.

Mr. ROGERS. That would be helpful.

Do you think such a practice is appropriate?

Dr. GOEPP. No, sir. In fact, I noted it because I don't think that should be done.

Mr. ROGERS. I presume that would be the basic ADA position on that. Would you let us know that for the record, too?

Dr. GOEPP. Yes.

Mr. ROGERS. What can ADA do to help correct that practice?

Dr. GOEPP. The American Dental Association has taken the view over 10 years ago that the radiologic examination of a patient is a unique decision based on the needs of the patient and directed to the welfare of the patient. In no way could that position be construed that one should do routine X-ray examinations. Nonetheless, there are still some schools; as I pointed out, there are some clinical settings and there are actually funding programs, some of them state welfare programs, which require routine examination of a patient in order to be paid for the service.

The patient may not need an X-ray examination. These are areas where I think attention should be directed.

Mr. ROGERS. Why does the ADA say that shouldn't be done?

Dr. GOEPP. It has said that.

Mr. ROGERS. To whom? If you would explain that to us, we would like to follow that up and be helpful.

Dr. STANFORD. The association has, through the publication of the Journal, said this to the membership and the Bureau of Radiological Health of the Food and Drug Administration. We have made that as a recommendation for the position of the council that it does not support this type of radiograph or radiographic procedure because it does not lend to the actual diagnosis of the patient's problem.

Mr. ROGERS. Would you put in the record a copy of the notification you have given so that we may have it as part of this record?

Dr. STANFORD. Yes, sir.

Mr. ROGERS. And we will try to take some action as well.

Dr. STANFORD. I will make the submitted material specific to this area. It is also part of the appended material in response to the questions you asked earlier, sir.

[The following information was received for the record:]

ADA POSITION TO THIRD PARTY REQUIREMENTS

The Association has published in the September 1976 issue of The Journal of the American Dental Association its position with respect to Third Party requirements. The following is quoted from the guidelines "The Association is opposed to any third party's policy or attempt to require mandatory submission of radiographs in every case, or in a blanket, automatic basis". A copy of the guidelines prepared by the Council on Dental Care Programs is appended. Appended also is a copy of the March 1978 "Recommendations in Radiographic Practices" from the Council on Dental Materials and Devices which includes the following: "The Council does not agree with a routine requirement of post operative radiographs to show proof of service rendered".

The Third Party

Radiographs: interpretation and duplication

The use of radiographs by third parties has been a controversial matter for several years

Guidelines on the use of radiographs were approved by the House of Delegates in 1972, and revised in 1974 Council interpretations of these guidelines were published in June 1974 (JADA 88 1234), at that time a relatively small number of dentists were involved with dental prepayment

Today some 30 million people are covered by dental insurance plans and that number is expected to double by 1980 Because more and more dentists are being involved in dental prepayment, there is a need to reemphasize the Association's position on radiographs

Eleven guidelines

The Association approves 11 guidelines on the use of radiographs in dental care programs

--The Association is opposed to any third party's policy or attempts to require mandatory submission of radiographs in every case, or on a blanket, automatic basis

—Radiographs shall only be used for determining the extent of liability of the program, and in no case should infringe on the professional judgment of the dentist or on the dentist-patient relationship

—Radiographs made by the dentist for his diagnosis are not the property of the patient or the third party, they are part of the dentist's records

—Intraoral radiographs shall be mounted

—Radiographs are only to be used to obtain information to clarify benefits the patient is entitled to under contract terms

—Radiographs shall be of such quality that they are properly diagnostic for clinical evaluation of the case involved

—Third party agencies shall not require postoperative radiographs unless it is a part of proper dental treatment, or for peer review purposes

—Radiographs shall be examined only by dentists

—Radiographs shall be returned to the dentist within ten days

—A third party agency that misuses records, either by making faulty judgments from such records, or by making determinations which could not ordinarily be made without proper examination of the patient in question, could be declared to have an unacceptable program Proper dental treatment is predicated on a diagnosis from many types of examination, and not from the radiographs alone

—Radiographs furnished to a peer review committee or third party shall not be transmitted to any other agency without written consent of the dentist

These guidelines have been studied and interpreted by the Council to offer clarification to dentists

The Association opposes any third party attempt to acquire radiographs for every case, or on an automatic basis In specific instances, when third parties do submit reasonable requests, the Association advises that dentists comply.

The Council cites two basic factors for determining what is reasonable The first is necessity Radiographs should be requested only when the dental treatment process has required them. Insurance considerations are secondary in this matter.

The second factor is that the radiograph should be requested only for the purpose of determining liability and clarifying benefits

A dentist's decision on whether to honor the guidelines may be determined on past experience Poor experiences, such as patterns of misuse by the requesting party, or unfulfilled obligations as determined in the guidelines may force a dentist to refrain from submitting requested radiographs The Council realizes that in these matters the dentist must make his own judgment However, when poor past experience is not the case, and the request meets the necessary conditions it is hoped that Association policy will be followed

In its study, the Council carefully examined typical requests for postoperative radiographs Peer review committees found these films very effective in determining certain matters within their jurisdiction, and this is identified in the guidelines

The use of postoperative radiographs for purposes other than peer review has frequently been disputed Although the Council recognizes a tendency to expedite solutions to problems encountered in validating claims, it stands firm in its position that radiographs should not be taken solely to satisfy the requests of the third party The Council emphasizes that radiographs should be taken only when they benefit the dental health of the patient Alternate monitoring methods should be used in determining the validity of dental claims when radiographs taken in the examination or treatment are nonexistent

Duplication of radiographs

Some dentists are hesitant to submit their films to third parties because the radiograph is a permanent part of a patient's dental record When a dentist submits an original radiograph for examination, he may be concerned that the film will be misplaced, lost, or damaged

In view of this, the Council canvassed several dentists experienced in prepayment, who offered suggestions for eliminating the small risk

One suggestion is the dual pack, which contains two films, one for the dentist's records, and one for the insurer, should he request it Although the dual pack is used and accepted by many dentists as a feasible solution to this problem, other dentists consider it an additional, unnecessary expense Dual pack film costs $13 to $15 for a packet of 50, as opposed to single pack film which costs $11 to $12

The purchase of a dental radiograph duplicator is a second potential solution to the problem A large selection of commercial duplicating equipment is available at a minimal cost of from $150 to $250

The final, and perhaps most economical, solution is for the dentist to make his own duplicator The necessary equipment—an 8 × 10-inch contact printing frame and a special autopositive film—can be bought inexpensively at most photography stores The frame costs between $10 and $15 (and a package of 50 single sheets of film costs about $11 to $12)

It is important to understand that lighting is a critical element of this process, and should be balanced for best results Even when this precaution is taken, however, the detailed reproduction is poor in comparison to that produced with the ultraviolet light boxes used in dental radiograph duplicators

Any questions concerning the Association's policy on radiographs should be directed to the Council on Dental Care Programs

REPORTS OF COUNCILS AND BUREAUS

Recommendations in radiographic practices—March 1978

Council on Dental Materials and Devices

The American Dental Association, through its Council on Dental Materials and Devices, has published a series of articles on radiation hygiene and practice. Beginning in the April 1967 issue of *The Journal*, articles have appeared on protection of the patient during radiographic procedures, protection of office personnel and dentist, modernization of X-ray equipment, use of fast-speed film, and proper darkroom procedures. An updated summary of Council recommendations is included here. In general, the Council's recommendations are a republication of its January 1975 recommendations and agree with those of other bodies in the area of radiation hygiene and practice.

Most of the recommendations are self-explanatory; however, the Council believes that some comment should be made on recommendation no. 1, on the frequency of radiographic examinations in dental practice. The American Dental Association has consistently stated that the use of X radiation for diagnostic purposes should be made only after careful consideration of both the dental and the general health needs of the patient. The deciding factor is the total welfare of the patient. The nature and extent of diagnosis for required patient care constitute the only rational bases for determining the need or the frequency of dental radiographic examination. The Council does not agree with a routine requirement of postoperative radiographs to show proof of service rendered. In other words, diagnostic radiography should be limited to those instances in which the dentist anticipates that the information he is likely to obtain will contribute materially to proper diagnosis, treatment, or prevention of disease, or all of these. The number of exposures to be made in the examination and the history of the patient's radiation exposure, especially to the head and neck, should be considered in making such an evaluation. The Council's recommendations follow:

1. Use professional judgment to determine the frequency and extent of each radiographic examination. Determine the minimum number of film exposures that will produce the desired diagnostic information.
2. The basis for film selection should be the maximum emulsion sensitivity (film speed) consistent with the image resolution (sharpness) required for the diagnostic task. Only film of an American National Standards Institute Speed Group "D" rating or faster should be used.
3. The tissue area (and volume) exposed to the primary X-ray beam (for each film) should not exceed the

minimum coverage consistent with meeting diagnostic requirements and clinical feasibility. When a cylindrically collimated X-ray beam is used, the beam striking the face should not be more than 2.75 inches (7 cm) when the source to skin distance is greater than 7 inches (18 cm) The beam should not exceed 2 38 inches (6 cm) if the source to skin distance is less than 7 inches (18 cm) Further restriction of the beam to reduce patient radiation exposure is preferred and can be obtained by smaller collimation such as rectangular collimation circumscribed by the aforementioned circular limits

4 The X-ray machine should contain a minimum total filtration consistent with federal and state requirements In general, total filtration should be equivalent to 1 5 mm aluminum up to 70 kilovolt (peak) and 2 5 mm for equipment operating above 70 kV(p) (More detailed information can be obtained from the Bureau of Radiological Health and state public health departments) The filtration should be located in the useful beam as near the X-ray source (focal spot of the tube) as is practicable Higher beam energy (kV[p]) allows decreased exposure, however, image contrast is reduced as energy increases, especially above 90 kV(p) Therefore, the maximum beam energy compatible with adequate image contrast should be used

5 Shielded open-end cylinders or rectangular-collimating devices should be used in conjunction with the long-cone technique. The combination of these devices and techniques will reduce the amount of scatter radiation reaching the patient's skin. All scattered radiation should be eliminated or contained, except for that occasioned by the passage of X rays through the tissues to reach the film

6 Expose the X-ray film properly Film exposures should be established for optimal density, using complete development Films should be processed under the film manufacturer's recommended conditions with proper processing equipment Image development should be extended to produce the maximum film density for the different X-ray exposures used without inducing significant chemical fog Overexposure corrected by underdevelopment subjects the patient and office personnel to unnecessary radiation and may result in loss of diagnostic information in the resulting radiographic image

7. Leaded aprons should be used on all patients to prevent unnecessary radiation of the gonads and thyroid glands

8 Never hold a film in place for a patient Use film holders, bite tabs, or other methods to position the film during exposure

9 Unless protective shielding is provided for the operator, the installation should be so arranged that the operator can stand at least six feet from the patient and outside the path of the useful beam when exposures are being made Work loads of more than 30 mamp minutes per week may require the use of an adequately shielded screen Information on shielding design, including determination of barrier requirements, can be obtained from "Dental X-ray protection NCRP report no 35," National Council on Radiation Protection and Measurements, Washington, DC, 1970.

10. State radiological health personnel or other qualified experts (see NCRP report no 35) should periodically conduct radiation protection surveys (including personnel monitoring quality control) of your office so that adequate measures can be taken to protect the health and safety of all patients and occupationally exposed personnel at all times.

11 Continue education in radiology as well as in other areas of dental practice

In essence, the decision to use diagnostic radiography rests on professional judgment of its necessity for the benefit of the total health of the patient. This decision having been made, it then becomes the duty of the dental professional to produce a maximum yield of information per unit of X-ray exposure.

Mr. ROGERS. Thank you so much. That will be helpful.

Dr. STANFORD. Mr. Rogers, may I add a statement?

Mr. ROGERS. Certainly.

Dr. STANFORD. A moment ago you asked about the radiologist and the teaching of the student. Again, as I indicated, I will obtain an opinion on the Council of Dental Education of the association for you.

I think it must be recognized, however. In part, that the request for the specialty which was included in the statement by Dr. Reiskin, I think should be commented on because I am concerned there might be a misunderstanding.

I think that it should be understood, sir, by the committee that it is not an action that has been taken so far by the house of delegates of the association in not approving a specialty for radiology and approving it as far as other areas of dental training. It is not a matter of it being a discrimination against the area of radiology. It was a moratorium on all specialties, the formation of any new specialties at all, and it was governed in part by the feelings of the profession, but also in part by the public who did not desire to see this diversification, this continuous making of a specialty in the area of dentistry; that they wanted to go to a person, dentist, who they could go to as a general person to take care of themselves as a patient and not have all of the specialty areas.

This is under continuous reexamination every year. I am sure our house of delegates will be considering it again. Therefore, for the record, it should be made clear, sir, it was not a discrimination against the area of radiology, as far as a specialty is concerned.

Mr. ROGERS. I can understand you might not want a radiologist in every dental office. I am not so sure but what you would want a radiologist teaching dentists. I think there is quite a difference.

I think we would like to have your comment on that for the record.

Dr. GOEPP. May I also speak to that issue, sir?

Mr. ROGERS. Certainly.

Dr. GOEPP. I agree with your last comment. In fact, that is part of what I wanted to say. My personal opinion is there should be some recognition for people who have developed expertise in radiology. Whether that is a specialty or whatever the label is, there must be some recognition.

My earlier comments, affirmative to this, were in the case of what you just described; the dental school. Certainly the teacher must be far more armed with knowledge than what the student is expected to know in order to practice. We must realize this moratorium exists not by some fiat or arbitrary decision. There is a public mood, frustration at being thought of as parts and pieces and the public is concerned to have one person to relate to, to be able to take care of them.

This has even been evidenced in action by Federal regulation or suggestion on the part of medical schools to train more general practitioners and train less specialists, and the ADA has gone along with that.

Mr. ROGERS. I think there is no disagreement on that.

I am thinking we are getting to the point of how they are trained, and probably 70 hours is not a sufficient training for someone who is going to make judgment on use of X-rays in many areas. And I expect when you have a radiologist who may take 3 years, not 7 days, or 10 hours or 8 days, 4 hours 1 day, 2 hours another for a total of 70 hours, but 3 years of training, then I question whether we are giving sufficient training to the general practicioner of dentistry on how to use X-ray equipment.

Dr. GOEPP. Yes. We must be careful with the term radiologist. We are not speaking of the general radiologists who raise from the medical profession. We are talking about radiologists who have expertise in the diseases of the mouth.

Mr. ROGERS. I understand.

We are also talking about someone who understands the effect, the health effects.

Dr. GOEPP. Yes, this would go with knowledge of the diseases.

Mr. ROGERS. And the fact one would know how to take a picture where three-fourths of them are not bad.

I just think we need your thinking on whether some change should be made in the qualification of those teaching radiology in the dental schools.

Dr. GOEPP. We have addressed some specific requests in our ancillary document.

[Testimony resumes on p. 666.]

[The following material was received for the record:]

QUALITY ASSURANCE IN DENTISTRY

In response to desires of the dentists as well as the public the association has prepared a report on "Quality Assurance in Dentistry" and a copy is appended. This report is a reslut of a contract to the American Dental Association with the Health Standards and Quality Bureau of the Department of Health, Education and Welfare.

Quality Assurance in Dentistry

Executive Summary

Joint Report of the Councils
on Dental Care Programs and
Hospital and Institutional
Dental Services and the
Bureau of Economic Research
and Statistics

As a health professional, each dentist is responsible to his patients for the care he provides. That responsibility includes proper diagnosis, appropriate treatment planning and the provision of care with a high level of competence. Beyond this individual obligation, the professional has generally cooperated with public agencies in safeguarding the public's oral health through activities such as aptitude testing of dental school applicants, accreditation of schools, licensure and encouragement of participation in continuing education.

The high quality of dental care that Americans enjoy is evidenced by the decreasing number of edentulous persons and the increasing use of preventive techniques. The quality of dental care received by Americans, however, has never been documented in detail. Nor have explicit quality assurance systems been implemented to demonstrate that the level of quality is what the profession believes it to be.

In July 1976 the American Dental Association entered an 18-month contract with the Health Standards and Quality Bureau (HSQB) of the Department of Health, Education, and Welfare to study current quality assurance activities in dentistry. Research efforts were directed toward identification of a dental quality assurance model that would be professionally created, professionally acceptable and responsive to questions currently being raised about the quality of dental care.

Definition of Quality Assurance: A search of the literature produces an assortment of definitions of quality assurance and related functions. For purposes of clarity, an attempt was made to synthesize several of the more prominent definitions.

> Quality assurance is the assessment or measurement of, or judgment about, the quality of care and the implementation of any necessary changes to either maintain or improve the quality of care rendered.

For the purposes of this project, a quality assurance system, also referred to as a dental care evaluation program (DCEP), is considered to be a method of evaluating the quality of dental care and includes the following steps:

1. selecting an aspect of dental care to be evaluated,
2. establishing criteria for quality dental care and making these characteristics of quality the standard for review,
3. comparing the care that has actually been given with the criteria,
4. making a peer judgment on quality based on the results of the comparison,
5. acting on the results of the evaluation to correct any deficiencies noted,
6. assuring that actions have favorable impact on the delivery of care by improving the normal delivery system through education.

This general outline of the steps in a quality assurance system must, of course, include specific factors such as the number of dentists and patients who will participate, the sources of information to be used, the approach to measurement of the care actually given and the follow-up actions.

A distinction should be made here between quality assurance and quality assessment. Quality assessment is the measurement phase of quality assurance and includes only the first four steps. Quality assurance goes beyond measurement and includes implementation of any necessary changes to maintain or improve the quality of care being delivered. This distinction is crucial for developing a system that will improve the delivery of care. The reasons for evaluating dental care focus on three areas:

1. supporting good dental practice through highlighting its efficacious and efficient elements,
2. identifying areas of dental practice that need improvement,
3. providing ongoing education to dentists and their auxiliaries about their practice.

The need for quality assurance systems in dentistry was heightened in 1972 by passage of the Professional Standards Review Organization (PSRO) legislation. This federal law is specifically directed toward monitoring at a peer level appropriateness and quality of care paid for under federal programs. Responsibility for implementation of the PSRO law at the federal level lies with the Health Standards and Quality Bureau (HSQB).

To date, PSRO review activities have focused on

BEST COPY AVAILABLE

care—including dental care—provided in institutional settings such as hospitals that is paid for under federal programs. However, as the PSRO program has gained experience in review of hospital care, it now expands its review authority—as the law contemplated—to noninstitutional (ambulatory) care. With this expansion, the dental profession will soon be faced with quality assurance activities under the federal mandate. The impact will be felt by private practitioners who deliver care that is paid for under federally funded programs as well as private prepayment programs.

Another factor contributing to the urgency for quality assurance in dentistry is the activity of the medical profession. Most of the research in quality assurance in medicine has been in terms of medical care delivered in hospitals. The hospital setting lends itself more readily to quality review than do private offices because of the centralization of practitioners, patients, and records, and the relative standardization of medical record forms. The medical field has been active in developing models of quality assurance and is currently moving, though cautiously, into quality assurance programs for ambulatory care.

A distinction should be made between quality assurance and peer review as it is commonly known in dentistry. Both utilize the concept of review of care by a group of peers. Either can be a vehicle for demonstrating high quality and for identifying problems in dental care. However, as currently understood, the peer review system is entered through grievances of either a dentist, a patient, or a third party, whereas quality assurance programs review dental care on an ongoing basis.

The Association's project had three objectives. The first, as mentioned, was to identify and describe quality assurance systems currently being used to evaluate dental care. These systems may be operating in hospitals, group practices, dental school clinical facilities, or private practitioners' offices. They also may be used by third party carriers. A second objective was to identify and develop quality assurance models that could be used for dental care evaluation. The model or models selected were to conform to the needs of dentistry and to requirements in the PSRO law.

It was anticipated that no single model would accommodate all delivery systems and that different models of evaluation would be required to correspond to different dental care delivery settings. The models were to be developed for possible field testing, although the field testing itself was not included in the contract between the Association and HSQB.

Third, the contract included development, by peer experts in the field, of sets of criteria for review of treatment procedures of four dental conditions, expected to be performed in hospital settings. These criteria could serve as screens with which the care actually given, as documented in the records, could be compared. Procedures that did not meet the screening criteria would be subject to peer review. Such criteria were to be used as guides for development within each PSRO, with appropriate, professionally designed modifications to reflect local practices.

Early contract activities focused on administrative and planning functions. This was through meetings with the project staff, composed of Ms. Susan Kahn, project director, Ms. Suzanne Morrissey, assistant project director, and Association resource staff composed of Dr. Helen Gift, Mr. Eric Bishop, Mr. Stephen Hardymon, Mr. John F. O'Donnell and Dr. Lowell Dunn. Ms. Jennifer Mauldin joined the project staff at a later date.

Core consultants representing the Council on Hospital and Institutional Dental Services and the Council on Dental Care Programs were selected and approved. These men served as the primary dental consultants to the project. Their clinical and practical expertise was invaluable.

Core Consultants

Dr. Joseph Kelly (Oral Surgeon), Chairman
Worcester, Massachusetts
Council on Hospital and Institutional Dental Services

Dr. William Booth (Orthodontist)
Sharon, Pennsylvania
Council on Dental Care Programs

Dr. Leon Eisenbud (Oral Pathologist)
New Hyde Park, New York
Council on Hospital and Institutional Dental Services

Dr. Sidney Francis (General Practitioner)
San Francisco, California
Council on Dental Care Programs

Dr. Emil Lanichner (General Practitioner)
Jamaica Estates, New York
Council on Dental Care Programs

Dr. Bernard Moran (General Practitioner)
Lincoln, Nebraska
Council on Dental Care Programs

The role of the core consultants was to:

1. provide input on review systems by evaluating them;
2. accompany project staff on site visits;
3. provide clinical expertise when scientific matters were involved, i.e., criteria development or review;
4. review drafts of plans, procedures and materials prepared by staff.

Methodology: The first step in identifying and describing a model quality assurance program for ambulatory dentistry was the compilation of a comprehensive list of review systems currently being used in or developed for dentistry. To accomplish this, a two-part data collection process was used. The first was a search of the medical and dental literature for information relevant to quality review.

The second information-gathering activity consisted of mailing a letter to the dental community introducing the project, delineating the types of data sought and requesting pertinent information. The letter was sent to the following:

BEST COPY AVAILABLE

1 all hospital dental services,
2 all group dental practices,
3 dental school deans,
4 state dental associations,
5 large component dental societies,
6 health maintenance organizations (HMOs) with full dental programs,
7 third party carriers (Delta dental plans, Blue Cross/Blue Shield, commercial carriers),
8 contact names provided by Dr. Joe T. Hillsman,
9 contact names found through literature review,
10 contact names obtained from other sources,
11 dental specialty organizations,
12 selected neighborhood health centers suggested by White et al in their study of ambulatory care.

Two hundred and thirty responses were elicited from the mailing, 98 were from hospital dental programs, and the others were from ambulatory settings and third party carriers. Forty-eight systems of quality assurance were identified as follows.

Hospital Review Systems

Alexian Brothers Hospital Review Procedure
California Medical Association Model for Patient Care Evaluation
Commission on Professional and Hospital Activities
Inquiry of Dental Audit—Long Island Jewish Hillside Medical Center (JCAH model)
Veterans Administration Systematic Internal Review Program

Ambulatory Review Systems

California Dental Association Task Force on Quality Evaluation
City of Houston Public Health Department—Dental Review
Cleveland Department of Public Health and Welfare
Connecticut Quality Assurance Program
Drew Ambulatory Care Review Team (DART)
Functional Task Analysis
Dr. Joseph Graves—Crown and Bridge, Inlay Index
Group Dental Associates P.C. Review System
Henry J. Austin Health Center
Hough Norwood Quality Review System
Indian Health Service, Dental Services Branch
Medical University of South Carolina Review
Medical Ambulatory Review System
New Jersey Dental Association Screening Criteria
New Mexico PSRO Review Procedure
Pennsylvania Dental Association
Philadelphia Department of Public Health
Prepaid Group Practice Dental Plan of Blue Cross of Wisconsin
Dr. Seymour Rostacher—Record Review System
Sunset Park Family Health Center
US Public Health Service, Region II
University of Mississippi School of Dentistry, Problem Oriented Dental System
University of North Carolina Dental Care Evaluation System
University of Pennsylvania Dental Care Evaluation and Quality Assurance Project
University of Washington—Assessment of Care and Continuing Dental Education
Virginia Dental Association
Washington, D.C. Neighborhood Health Center

Third Party Carrier Review Systems

Aetna Life & Casualty Company
California Dental Service*
Connecticut General Life Insurance Company
Delta Dental Plan of Michigan
Delta Dental Plan of Tennessee
Delta Plan, Salt Lake City, Utah
Group Health Association, Inc
Group Health Incorporated
John Hancock Mutual Life Insurance Company
Maryland Dental Plan
Metropolitan Life Insurance Company
Michigan Blue Shield
Missouri Delta
New York City Bureau of Health Care Services
New York Medicaid Dental Rehabilitation Program
The Travelers Insurance Company
U.S. Administrators

The next step in this initial phase of the project was to develop an instrument that could be used to objectively compare systems and aid in the selection of systems to be reviewed in depth. The parameters selected were those that best identified systems whose goals were congruous with the goals of the project, i.e., to identify models of review of dentistry that look at the necessity, appropriateness and quality of dental care and meet the specifications of the Professional Standards Review Organization program. In addition, the parameters chosen were those that could be assessed without an in-depth study of each system.

In order of priority, the characteristics chosen were

I goal of the system
II completeness of the evaluation,
III activity level,
IV replicability in other dental settings,
V dentist-nondentist participation

For each of these items a set of comprehensive and mutually exclusive criteria was established based on a scale of one to four. Each of the items received a weight based on its priority as follows

Rating received on Item I × 4
Rating received on Item II × 3
Rating received on Item III × 2
Rating received on Item IV × 1
Rating received on Item V × 1

After testing for inter-rater reliability, all the systems were rated and scored and then were compared within categories (hospital inpatient review, ambulatory review and third party carrier review) so that, for example, each inpatient model of evaluation was compared only with other inpatient review methods.

Each system, having been summarized and rated within setting category, was then classified as to its setting—ambulatory setting, third party carrier and fourth party carrier—and its principal data source.

Record review only

---

*Information about this system was obtained late in the project, it was not included in the rating or selection process.

BEST COPY AVAILABLE

Clinical evaluation only
Data utilization only
Record review and clinical evaluation
Clinical evaluation and data utilization
Record review and data utilization
Record, clinical and data utilization

In addition, a special category, "Criteria only," was established to provide for programs that had developed criteria but have not established a protocol for using the criteria. This classification was done so that the similar systems of review could be compared to one another and representatives from the many varied approaches to review could be examined in depth.

The ratings received together with the comments of the core consultants and expert opinion were considered in selecting nine systems for in-depth review. Each system selected was the best representative of the various data sources and combination of sources.

Inpatient Hospital Review

Record Review	Inpatient Dental Audit (Performance Evaluation Procedure) Long Island Jewish Hospital Hillside Medical Center New Hyde Park, New York

Ambulatory Review

Record Review	Drew Ambulatory Care Review Team (DART) Los Angeles, California
Data Utilization (Program Data)	Neighborhood Health Center Review US Public Health Service, Region II New York, New York
Record Review and Clinical Examination	University of Mississippi School of Dentistry Problem Oriented Dental System Jackson, Mississippi
Record Review and Data Utilization	Dental Care Evaluation and Quality Assurance Project University of Pennsylvania Department of Dental Care Systems School of Dental Medicine Leonard Davis Institute and the National Health Care Management Center Philadelphia, Pennsylvania
Record Review, Clinical Examination and Data Utilization	Indian Health Service Dental Services Branch Albuquerque, New Mexico
	Dental Care Evaluation Program Dental Demonstration Practice Dental Research Center University of North Carolina at Chapel Hill Chapel Hill, North Carolina
	Dondis/Rosenthal Review System Sunset Park Family Health Center of the Lutheran Medical Center Brooklyn, New York

Third Party Carrier Review

Record Review, Clinical Examination and Data Utilization	Delta Plan (Utah, Nevada and Montana) Salt Lake City, Utah

In addition, two systems were chosen to be reviewed as addenda to other systems. The first of these was the U.S. Administration's program of review which was chosen as an addendum to the third party review because of its role as a fourth party. It was thought that since a different level of implementing review programs is involved, attention should be given to the program's specific activities. The other system, an addendum to the combination record review, clinical examination and data utilization types of review, was the Connecticut Quality Assurance Program which includes Dr. Howard Bailit's research in quality assurance.

After the selection of the systems to be studied in depth, an instrument to collect the descriptive information was developed as an aid during the site visits which were conducted on nine of the eleven systems.

A proposed site visit agenda was prepared so that the participants could discuss the quality assurance program and actually watch or, in some cases, participate in the review process. The usual site visit agenda included, on the first day, discussion of the project, thorough review of the completed data collection instrument and subjective discussion of the review system. On the second day, the project staff saw the various steps of the review system being implemented and closed the visit with final questions and discussion.

Six weeks before each visit, the data collection instrument (DCI) was sent to the contact person who was instructed to complete all sections relevant to the review system and to the site. He was allowed to gather necessary information from appropriate personnel, but he was in charge of actually completing the DCI. He was asked to send copies of the completed DCI two weeks before the visit to the project staff and the consultants who would be attending. Approximately two weeks prior to each visit, the proposed agenda was sent to the contact person. This gave him an opportunity to change the agenda if necessary before the actual visit.

Nine site visits took place between the months of February and June 1977. Attempts were made to include one core consultant on each visit.

After the site visits, detailed reports describing the systems were prepared as were flowcharts to identify the decision making points in the systems. Tapes of the visits, completed DCIs and written documents provided by the sites served as the basis for these reports. Upon completion, each draft report was sent to the site contact person for verification. In most cases, others participating in the site visit were given the opportunity to review and comment on the draft. Final reports were then prepared.

Because it was felt that no quality assurance system can be effective unless it has the approval and support of the dentists whose care is being examined, the input of practicing dentists representing dental specialties and

BEST COPY AVAILABLE

interests was sought. The project staff compiled a list of consultants to review the summary reports. All dental specialty organizations and many special dental interest groups were asked to name one of their members to serve as a consultant to the project. The groups that responded and their representatives were:

American Association of Orthodontists, Dr. C. Moody Alexander
American Academy of Periodontology, Dr. John F. Dierksmeier
Federation of Prosthodontic Organizations, Dr. Daniel H. Gardner
American Association of Hospital Dentists, Dr. R. Pat Helton, Jr.
American Association of Oral and Maxillofacial Surgeons, Dr. N. Robert Jones III
American Dental Hygienists' Association, Dr. Linda P. Joseph
American Association of Public Health Dentists, Dr. Richard F. Murphy
American Academy of Pedodontics, Dr. Robert J. Musselman
American Association of Endodontists, Dr. Arthur C. McKeavers, Jr.
Academy of General Dentistry, Dr. Eugene J. Truono

In addition to these specialists, the list of consultants included Drs. James E. Lassiter, Jr., Frank L. Shuford, Jr., Dolores M. Franklin Suggs, Major W. Tappan and Edgar E. Cooper.

These 15 consultants received summary reports of the nine quality assurance systems for which site visits were made. For each report, the consultants were asked to consider the following questions:

1. Is any part of the system unclear? Should any other questions regarding the system be answered?

2. Which of the systems may be appropriate and feasible for dental quality assurance and which may not?

3. Which parts of any system may be appropriate and feasible (with or without modification) for dental quality assurance and which may not?

4. What modifications might be needed in any system or parts of the systems to make them workable, especially in the solo practice setting?

After all the data were collected and summary reports prepared, it was evident that a summary of the most pertinent characteristics would be appropriate. The chart would describe the state of the art as it had been examined through the site visits. Because of the comprehensive nature of the two addendum reports, a decision was made to include them.

The factors selected to be described were, in part, contractually defined, but to a greater extent, they were selected because they described key items that distinguish various approaches to review. The factors selected along with the questions that were asked for each factor follow.

Classification Factor	**Questions Asked**
Organizational structure	In what type of setting is the DQAP operating?
Types of review	What is the general approach of the DQAP?
Time of review	At what point in the treatment process is care evaluated?
Population reviewed (sources of payment)	Which portions of the patient population are subject to review?
	Which reimbursement sources are represented in the patients subject to review?
Internal-external review	Is review conducted by in-house staff or are those conducting review external to the site reviewed?
Areas of review	What aspects of total patient care are examined?
Type of utilization review	What aspects of utilization of dental services are reviewed?
Dental services reviewed	What categories of dental care services are reviewed?
Frequency of review	How often do review activities occur (complete studies)?
Type of personnel reviewed	Which type of staff members have their performance reviewed?
Basis for topic selection	What determines the aspects of quality to be reviewed?
Basis for provider selection	How are providers selected to have the care they render reviewed?
Basis for case selection	How are individual cases (e.g., patients, patient record, claim-encounter form) selected to be reviewed
Use of criteria (either implicit or explicit)	Does the system utilize some type of predetermined measure?
Focus of criteria	Do the criteria measure structural aspects of the practice, process of care or outcome of care?
Sources of criteria	What sources of information are used in criteria development?
Type of standards	Are standards empirical (based on experience) or based on expert knowledge?
Data sources used	What are the primary types of sources used to gather information about quality?
Use of codes	Are any codes used in the DQAP? What are they?
Type of data abstraction	Are the data collected and tabulated manually or is a computer used?
Personnel used in data abstraction	What type of person (by title) collects the data for review?
Type of data analysis	Are individual variant cases, aggregate data, or both reviewed?
Personnel used in data analysis	What types of personnel (by title) are involved in reviewing and analyzing the data?
Corrective action emphasis	What types of corrective actions have been or could be implemented as a result of a review finding?

BEST COPY AVAILABLE

Classification Factor	Questions Asked
Appeals mechanism	Does the system have a formal program for appeals of adverse review decisions?
Type of follow up	What is done to assure that recommended actions have been taken and are effective?
Type of reporting requirements	What portions of the review are to be documented?
Time spent in review by dentist	Approximately how much time is the dentist devoting to the DCEP (per review if possible)?
Time spent in review by nondentist	Approximately how much of non-dental personnel time is devoted to the DCEP (per review if possible, excluding computer time and personnel)?
Integration with other forms of review	How does the DCEP relate to other forms of ongoing review of the practice or program such as PSRO, third party review, peer review, Medicaid review, etc.?
Available impact data (formal informal)	Is there any formal or anecdotal evidence that implementation of the DCEP has favorably influenced dental care through change in dental health status, provider behavior, practice management or improved resource utilization?
Confidentiality provisions	Are there assurances that all materials used in the DCEP are confidential?
Test for provider satisfaction	Has the acceptability of the DCEP and its effect on the providers examined been evaluated?
Initial costs	What total start up costs (implicit and explicit) were incurred initially that will not be repeated? Include development of computer capability
Implementation costs	What are the explicit and implicit costs specific to the operation of the DCEP?
Cost per study	What are the costs per patient reviewed or per provider reviewed?
Evaluation of system	How many of the system's components are periodically assessed and revised?

Information for the classification was obtained through summary reports, data collection instruments, tapes of the site visits and written documents provided to staff.

Because the classification placed no value judgment on the description of any one system within a characteristic, a Quality Assurance Model for Dentistry was developed, which describes 97 items considered to be ideal characteristics of any system of quality assurance. These broad characteristics provide a more detailed examination of each system as well as a more systematic assessment of each program.

A review of the literature on dental quality assurance indicates that various approaches to review have been discussed (Bailit, Sowell, Ryge, Morehead) as have general concepts related to parts of review, pros and cons of the review approaches and criteria development. However, except for the work of Hillsman[8] and Schonfeld,[9] basic, essential characteristics and components of a quality assurance system had not been addressed.

Because one goal of this project was to describe the state of the art, it seemed appropriate to describe that state according to parameters perceived by experts to be critical issues in quality assurance systems. To do this, an instrument was developed which could more objectively assess the elements of quality assurance and identify areas requiring more development.

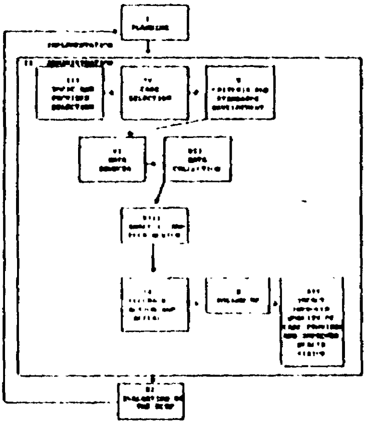
The model that was developed identifies 12 major *elements*, essential subject areas to be addressed in any quality assurance system. Within each element, *characteristics* were identified. These were described in terms of methods and procedures to accomplish various tasks.

The draft of the model was sent to 22 consultants, including dentists, physicians, and others with experience in quality assurance. Extensive revisions were made based on the comments received from consultants and the final model was prepared (Figure 1).

The 12 major elements selected were based on what has generally been defined by others to be the primary

FIGURE 1

QUALITY ASSURANCE MODEL FOR DENTISTRY



BEST COPY AVAILABLE

areas to be developed, planned and operationalized in a system for quality assurance. They are as follows

I Planning
II Administration of the System
III Topic and Provider Selection
IV Case Selection
V Criteria and Standards
VI Data Sources
VII Data Collection
VIII Analysis and Peer Review
IX Feedback, Action and Appeals
X Follow up
XI Evaluation of the Review System
XII Impact of Review

Each of elements III-X follows directly from the previous one. Choosing a topic, selecting the cases and providers to be reviewed, establishing the measures, performing the measurement, analyzing the results, taking action based on the results and following up to assure action has been implemented represents the usual sequence of events when evaluation takes place.

The planning (element I) and preparation for implementation of the system affects each of the elements as does the administration (element II). Without proper planning and administration, the program may not run as effectively as possible. The system itself and each of its components must constantly be assessed for its adequacy as a method of achieving the goals of review. Therefore element XI, evaluation of the review system, feeds into all other elements and necessary revisions must be planned (I), administered (II) and operationalized (III - X). Finally, if all parts are properly operating, the quality assurance system itself must achieve its ultimate goal, which is to impact positively on provider behavior and ultimately on the health status of the patients. Element XII suggests that in the ideal program there is definite impact on the quality of care.

While the elements identify the essential components of review that must be addressed, the characteristics within each element identify objectives in the form of procedures and methods which ideally should be achieved to indicate that the element has been covered adequately. Although these characteristics can be achieved in a variety of ways, it seemed important to those developing and reviewing the model that each system demonstrate them to reflect a comprehensive review process.

In establishing the characteristics under each element, several questions were considered

1 Did it identify a characteristic which ideally should be present in a system regardless of approach?

2 Was it one that required thorough planning and implementation?

3 Was it consistent with a systematic and comprehensive evaluation program?

4 Were there adequate data available to make a judgment?

5 Was it capable of being modified at a later time (e g , quantified to examine degree of compliance)?

6 Was it consistent with general provisions for PSRO review in ambulatory settings?

7 Was it acceptable to the dental profession?

The model for quality assurance in dentistry follows

I The Planning

The quality assurance system has procedures or methods to
A Include review of the literature in initial development
B Define goals of the system
C Utilize input from practicing dentists in the development of the system
D Solicit advice from expert technical and clinical consultants when necessary
E Plan a definite budget for quality assurance activities
F Discuss the system's approach with the dental and support staff who will be implementing the system
G Assure the system functions in an established organizational structure
H If more than one approach is used, define the interrelationships among the types of review
I Fully document all procedures in the system
J Replicate the system in more than one type of setting
K Determine the cost effectiveness of the system
L Pilot test the system
M Build in incentives to encourage provider and support staff participation
N Utilize an educational rather than a punitive orientation

II Administration of the System

The quality assurance system has procedures or methods to
A Assign tasks to staff members conducting review
B Formally train those who will implement the system
C Define the organizational structure with lines of communication and authority delineated
D Identify reporting requirements
E Assure confidentiality of all materials (e g , patient records, data reports, review decisions, peer review discussion content)
F Assure review activity is ongoing in nature (specified at regular intervals)
G Define sanctions for noncompliance and authority to apply them

III Topic and Provider Selection

The quality assurance system has procedures or methods to
A Identify topics for review (i e , diagnosis, dental procedure, problem)
B Select topics which will be reviewed (topic specific)
C Solicit input from providers for topic selection
D Select providers who will be reviewed
E Inform providers their performance is under review

IV Case Selection

The quality assurance system has procedures or methods to
A Identify the method of case selection
B Select cases in the form of patient records, claim forms, encounter forms or patients which are representative of all patients relative to the topic under study
C Select cases representative of providers under review
D Select cases which reflect current practice

V Criteria* and Standards**

The DCEP has procedures or methods to

---

*Criteria—predetermined statements that define elements of care to be used as indicators of quality

**Standards—numerically expressed frequencies which identify the range of acceptable variation from a norm or criterion

BEST COPY AVAILABLE

A Utilize criteria and standards
B Assure criteria are explicit and measurable
C Assure peers, representatives of the providers to be reviewed, develop the criteria
D Base criteria on experience and/or peer accepted expert advice
E Assure criteria are applicable to the topics, cases, providers reviewed
F Assure criteria are applicable to the data source(s) available
G Define all terms in the criteria
H Assure explicit criteria measure, among other things, necessity of care (need for treatment in first place)
I Assure explicit criteria measure among other things quality and effectiveness of care
J Assure explicit criteria measure, among other things, appropriateness of care
K Assign standards to criteria
L Test criteria and standards for validity
M Test criteria and standards for reliability
N Assure use and meaning of criteria and standards are understandable to those using them
O Afford providers under review an opportunity to review the criteria and standards

VI Data Sources

(patient record, claim form, patient)

The quality assurance system has procedures or methods to
A Select data sources to be used to review quality
B Test the data sources for validity
C Assure easy access to the data sources for purposes of ongoing review
D Assure that the dentist/patient relationship is not disrupted in the selection and use of the data source

VII Data Collection

The quality assurance system has procedures or methods to
A Define the data collection process
B Test the method of measurement used for reliability (inter- and intra-rater reliability)
C Utilize nondentists to the extent possible to abstract data, not requiring clinical decision making
D Assure use of dentist for decisions in data abstraction requiring clinical expertise
E Assure data can be collected and retrieved over time
F Define any weighting that is used in scoring
G Define any codes utilized
H If codes are used, incorporate prevalent professionally accepted codes whenever possible (e.g., ADA Code on Dental Procedures and Nomenclature)

VIII Analysis and Peer Review

The quality assurance system has procedures or methods to
A Conduct review of individual variant cases
B Conduct review of aggregate data
C Assure that all final judgments about the quality of dental care are made by dentists (other peers may be appropriate in special cases, for example, dental hygiene procedures)
D Subject all variant cases to peer review or else provide documentation of the special provisions for exclusion of cases
E Assure reasons for case variation are reported in writing
F Assure that all ultimate judgments related to the quality or adequacy of care rendered are made by more than one dentist (true peer review)
G* Assure controls for reviewer bias
H* Assure all relevant data including records and data abstraction reports are available for peer review
I* Assure additional information for peer review will be available if necessary
J* Assure peer review decisions are reported in writing
K Assure that reports of the review and analysis will be forwarded to appropriate sources (i.e., governing bodies, board of directors, dental directors)

*Items G, H, I and J receive two scores—one for individual case review and one for aggregate review. All others refer to procedures for both types of review.

IX Feedback, Action and Appeals

The quality assurance system has procedures or methods to
A Assure feedback to the appropriate parties
B Assure positive as well as negative feedback is communicated to the appropriate sources
C Assure that all feedback is timely
D Assure immediate feedback when a deficiency represents a danger to the patient
E Recommend corrective action related to review to the appropriate source
F Assure that recommended actions are reported in writing
G Appeal review decisions
H Inform all those under review of the appeals mechanism

X Follow up

The quality assurance system has procedures or methods to
A Assure recommended actions taken were appropriate and implemented
B Assure responsibility for follow-up activities is defined
C Test the impact of the actions taken on the correction of the problem (restudies, concurrent monitoring, etc.)
D Implement further action if necessary to correct remaining deficiencies

XI Evaluation of the Review System

The quality assurance system has procedures or methods to periodically assess and revise when necessary
A The administrative aspects of the system
B The method for topic and provider selection
C The method for case selection
D The criteria and standards used
E The data sources used
F The method for data collection
G The method of data analysis and peer review
H The methods for feedback and recommending corrective action
I The methods for follow-up
J The costs of the program

The quality assurance system has procedures or methods to
K Review provider satisfaction with the quality assurance system

XII Impact of Review

The quality assurance system has procedures or methods to
A Demonstrate maintenance or improvement of provider behavior since quality assurance system implementation (e.g., improvements in resource utilization, task performance)
B Demonstrate maintenance or improvement of dental health status since quality assurance system implementation

The model was developed to provide a systematic approach to examine dental quality assurance systems. It provides a method to assess one system against ideal characteristics of quality assurance as identified by experts in the field.

The model can also be used to compare one quality assurance program to another. However, because of the nature of this study in which a variety of settings and diverse approaches to review are examined, it is difficult to make comparisons. For purposes of the present study, the model was considered most valuable when the quality assurance systems were examined across each

BEST COPY AVAILABLE

characteristic. Those items that did not appear to be adequately addressed by the systems studied were identified.

Findings: Some very general findings relative to the elements in the model are described below as basic background to the recommendations made in the study.

Planning. Goals for the systems reviewed were well thought out and delineated. Systems had a definite place within the organization's structure, and documentation of each protocol was either completed or initiated.

The programs, for the most part, operated as educational rather than punitive programs. Practitioner input in developing most systems was evident, as was interaction with support staff. Additionally, the quality assurance programs themselves were, in some cases, the feedback for identifying problems in dental care which required educational programs to rectify.

Cost information was scarce, although enough cost data were available to determine that it generally costs less to use indirect measures of quality evaluation such as record review than to use direct measures such as clinical examination. Indirect measures can more readily use nondentist personnel, which keeps the cost of salaries for a review down. They also allow the use of screening techniques, which may mean more cases can be evaluated and can reduce the number of dentist hours required.

Administration of the System. Formal training used in these programs was noted for the range of activity from highly structured, in-house week-long seminars to none at all.

The problems of confidentiality of data were examined with most programs at least cursorily addressing provisions to assure confidentiality, yet three of the programs had not addressed it at all.

Topic and Provider Selection. For the most part, the 11 quality assurance systems were not purposely selecting quality study topics on which to focus review, although all but one have mechanisms to identify potential review topics. Only the inpatient hospital audit uses a topic-specific approach to review.

Many programs reviewed whatever was found in the record, patient or claim form examined. Some programs did use input from those under review as a basis for choosing areas needing review.

Selection of practitioners to review varied with the size of the program, but generally all programs were able to at least annually review some aspect of each practitioner participating in the program. Many of the systems reviewed the care rendered by dentist and auxiliary staff, however, six solely addressed the dentist.

Case Selection. Some programs randomly select the cases to be reviewed, while others review only cases seen on the day of a site visit, all cases seen for a particular topic, *all* cases or focus review on cases where potential problems have been identified.

Criteria and Standards. The diverse nature of the measures used to evaluate quality in the 11 programs of quality assurance is striking. The focus of the criteria, the aspects of quality to be reviewed and the procedures to develop criteria also vary.

Criteria used in the quality assurance systems examined focused on all three major areas—structure, process and outcome.

Structure Criteria. These criteria refer to aspects of the organization and resources that support the provision of dental care.

Process Criteria. These criteria describe the procedures or therapies performed and the management of the disease. In all systems examined, process criteria were emphasized. Although many items of process can be identified using claims-based and encounter-based data, records appear to be used the most widely. Generally, performance in taking a history, diagnosis, examination, treatment plan and treatments is measured using the record.

In identifying process criteria (as well as other criteria), an implicit or explicit approach can be taken. Explicit criteria are predetermined, specific and measurable. They require little judgment to assess compliance. Implicit criteria use a less specific approach that calls for subjective judgments to determine compliance. The latter type of criteria are predominant in dental review, particularly when indirect data sources (e.g., record, claim form) are used.

Outcome Criteria. These criteria express the desired conditions as a result of treatment. This is the focus of the inpatient audit system.

Ambulatory settings have more difficulty in describing outcomes of dental care because an outcome may not be fully realized for a long time. However, care that was performed many years ago frequently does not reflect current practice patterns. Also, because of many outside factors, long-term outcomes are difficult to measure adequately. Such factors may be totally unrelated to the provider's performance.

The problem of making the criteria more objective was discussed frequently during the site visits, particularly in relation to examining appropriateness of care through the treatment plan and the record. Because the possibilities for decision making are vast, objective measures are difficult to establish.

Determination of the aspects of dental care to be reviewed depended to some extent on the data source selected in a particular system of review. For example, the measurement of technical quality required clinical examination, measures of the necessity of treatment required baseline data. Utilization patterns were best extracted by reviewing claims-based or encounter-based data. Other aspects of care and practice assessed included productivity, effectiveness, oral health status, appropriateness of treatment planning, completeness of record, costs of care, patient satisfaction, acceptability of care, appropriateness of care and access to care.

The criteria used in each of the systems were generally developed internally by peers; however, most have not been tested for validity (examining whether the

BEST COPY AVAILABLE

item actually measures what it is supposed to measure) and reliability (determining whether it is possible to use the criterion twice and obtain the same results)

Data Sources and Data Collection Three principal data sources were found clinical examination, record and claim form although direct observation, questionnaire and personal interview are other sources used

Four of the eleven systems incorporate the clinical examination as a first level review mechanism, and two use the clinical when decisions cannot be made using other sources

Although clinical examinations are the best measure of technical outcome of treatment, they were found to have several limitations First, measurement of technical quality implies a narrow definition of quality Furthermore, since clinical examinations must be performed by dentists, they are a comparatively costly type of review compared to those in which nondentists can be used for much of the review Time commitment by dentists ranged from eight minutes per exam to 40 minutes per exam with costs ranging from $50 to $500 per dentist reviewed

Generally, the clinical examinations are performed at the facility where care was originally provided, but this is not always the case

Eight of the programs included some form of record review in their quality assurance programs For seven of these, record review takes place on two levels The first level is the explicit determination of whether certain information is documented in the record, this has been conducted, in some cases, but by a nondentist The second is the implicit evaluation of the appropriateness of care as documented in the record Because of the absence of explicit criteria, it is generally accepted that dentists should perform this portion of the evaluation

No specific research has been done to determine what constitutes a typical clinical record or what information should be documented to evaluate quality of care through record review

However, there are indications that the information available from the treatment record may be significantly limited Dr Howard Bailit found that the "average" record is adequate only for reviewing the actual services received by the patient

Data utilization or profiling is an approach to review of dental care that generally, though not necessarily, involves computers Eight of the 11 review systems had some degree of computerization Through development of adequate information systems by collection of claims data or encounter data or by compilation of daily logs, review of data can be accomplished to identify patterns of behavior and patterns of care through a profile For this study, a profile was defined as aggregate data in formats which display patterns of health care services over a defined period of time

Data utilization can examine an individual provider or an entire program Although most systems emphasize the former, one focused on program review

The most familiar type of profile is that compiled using claim forms Profiles may identify a provider and look at all the treatments rendered, identify a specific treatment and examine it in all the dentists providing it, or identify the treatment history of a single patient By storing the data collected on the claim form, profiles can be generated for review across providers, patients, treatments, payment classification or any other factor for which data are available.

Other profile systems reviewed focused on use of encounter forms which include data items not found on the claim form and considered useful for practice management and evaluative purposes Such things as a diagnosis, type of visit, completion status and measures of oral health status were included on these encounter forms.

The desirable aspect of profiles based on claim form and encounter form data is that the dentist is required only to review an identified problem The data from the forms are generally completed by auxiliary office staff The data are entered by computer personnel, and the reports are analyzed to point out what appears to be aberrant behavior This identifies the focus or the target for in-depth review

Analysis and Peer Review After data are collected through examining a patient or by comparing the record or profile to criteria, the cases that do not conform to the criteria may require review and analysis in more depth The systems studied had different methods to identify and analyze these variant cases.

The use of dentists to make quality related judgments, and assuring that more than one dentist is making the final judgments about quality, are important characteristics of a quality assurance system Utilizing more than one dentist for final quality decisions prevents review from being a one-on-one process Seven of the selected systems provided for clinical quality judgments by dentists True peer review by using more than one dentist's decision was the case in four programs

Even using peer committee structure, little emphasis had been placed on the problem of controlling for reviewer bias When consensus decision making is required, some of the problem diminishes, but in programs that use one dentist for decision making, the problem becomes more critical

Feedback, Action and Appeals After data review and analysis findings must be made known to those reviewed and any necessary action recommended Without these steps, all previous steps are only an exercise Assessment does not assure quality Changing problem provider behavior requires knowledge and awareness of the problems Furthermore, review should be geared not only toward problem finding but toward demonstrating good quality as well Both positive and negative findings need to be made known

All of the systems examined assure negative feedback to the provider However, in six systems, feedback of positive review results is informal

Some feedback is done immediately by personal contact, others use formal written communication Feedback may be delayed due to administrative review in some programs All programs did have provisions for

BEST COPY AVAILABLE

immediate feedback if a deficiency in care endangers the patient. One program sets up an appointment immediately for any patient found to have a problem in the technical quality of his dental care.

Recommended actions are reported in writing, and all the systems have reporting protocols to assure that recommendations are forwarded to the individual responsible for implementation. Actions taken by the programs varied from education to dismissal.

Appeals programs were part of six of the systems, three of which have appeal to a committee.

Although all of the systems have formal procedures for action and although two systems have dismissed dentists who were delivering poor quality care, there has not been enough experience in conducting quality assurance systems to determine the degree to which punitive actions will be enforced. Experience in some areas of quality assurance, such as institutional review, has shown professional reluctance to enforce actions against peers. The difficulty arises when actions related to limiting or reducing privileges are deemed necessary. This problem has been identified time and again and seems to be the point at which many review systems break down.

Follow-up. Follow-up activity was evident in eight systems. Some assigned responsibility for the follow-up, while others used the dentist to take the initiative to report when corrective actions had been taken.

Whereas checkup visits or self reporting of corrective actions are appropriate for administrative changes, changes in treatment patterns of provider behavior require monitoring over time. Most of the systems recognize this and plan to look at audit results over time to identify change. One program used a mini study that focused on the identified problem to assure changes had occurred.

Evaluation of the Review System. Some of the major aspects of a quality assurance system that should be evaluated are goals and objectives of the system, duties of personnel, process of selecting services and providers to review, the use of dental records, claim forms and encounter forms, use of criteria, methods of review and analysis of data, action and follow-up programs and the use of computers. No pattern was discernible in quality assurance systems that were studied. Some evaluation was on an ongoing basis, other review was done monthly, quarterly, annually, etc., or in some cases not at all.

Impact of Review. Little work has been done in the area of assessing the effects of a quality assurance system on patients, providers or the dental program or practice itself. Almost all that is being done is informal.

Measuring the impact of review on the quality of dental care and on the oral health status of the patient population is extremely difficult. The study sites did not provide substantial demonstration that review had significantly affected provider behavior or that the oral health of the patients had improved.

What may be an even more significant measure of a quality assurance program is the cost effectiveness of the program. Expenditures for review activities were extremely difficult to obtain, only two of the nine systems had planned a definite budget for evaluation programs.

The lack of activity in this area is not surprising for two reasons, both of which are related to the newness of the programs (most had been operational less than two years). First, much of the initial effort in a quality assurance system is generally directed toward establishing and testing the procedures to conduct review. Resources are not directed toward assessing the effectiveness of the system in improving the quality of care. Second, any real changes in provider behavior or oral health status require considerable time to discern.

Recommendations for Policy Consideration and Further Research Needs: Analysis of 11 quality review systems and discussions with quality assurance experts and dental practitioners have raised many questions about the future of quality assurance in dentistry. The project staff has prepared a list of recommendations for policy considerations and further research needs. The recommendations are presented according to the components of the Quality Assurance Model for Dentistry. A fuller understanding of the basis of these recommendations is found in Volume I of the final report.

Planning

Policy Considerations: Appropriate incentives to encourage dentist participation in quality assurance activities should be identified. Providers' needs and perceptions relative to these activities require assessment.

A budget is an important characteristic of a quality assurance system. The exclusion of a budget precludes another important item, determining the system's cost-effectiveness. A planned and monitored budget should be included so that costs can be weighed against benefits accrued. Then it will be possible to identify the best results obtained for the amount of money expended.

Further Research Needs: Quality assurance activities in solo practices have been limited, and the applicability of existing systems to this setting should be explored. Replication is needed in a variety of solo practices.

Relationships between quality assurance and continuing education programs should be explored. Milgrom's research indicated a significant relationship between quality of care and perceived usefulness of university courses and study clubs.[4] Further, participation in quality assurance activities should be considered a form of continuing education, and provisions for credit should be made.

Administration of the System

Policy Considerations: Examination and discussion are needed to determine what types of information should be documented and who should be required to see review reports in a quality assurance program. Then specific guidelines to assure confidentiality of reports and the completeness of the review cycle must be developed before review and should be made known to all who are being reviewed.

At the time of implementation, a review system

BEST COPY AVAILABLE

should have specified frequencies of occurrence, and the integration of the system in the practice structure should be defined clearly. Regularly scheduled review that is integrated well into office activities enhances the review's importance, whereas an unstructured, haphazard approach may not.

Topic and Provider Selection

Policy Considerations: Review systems should be able to accommodate assessment of all types of dental care practitioners.

Further Research Needs: Separate studies by Brook in medicine[5] and Hardt in dentistry[6] show that there may be little variability in the quality of health care services within a practice. Identification of the quality of the most frequently provided services may be indicative of the quality of all services. Studies are needed to determine the variability within a dental practice among treatments rendered. In this way a sample of cases for which sufficient data can be gathered to yield meaningful results will be identified.

Case Selection

Further Research Needs: Although it may not be practical to select a genuine random sample for each audit, the sample should be representative of the quality of care rendered in the practice. An expedient, valid selection process should be developed to provide the most meaningful results.

The variability within a practice in performance of a single treatment or in treatment planning needs to be identified so that an appropriate minimum sample size can be determined regardless of the approach to review.

Criteria and Standards

Policy Considerations: Until a national system is identified, thoroughly field tested, and found to be an effective and acceptable mechanism for review of the quality of dental care, criteria should be developed locally for each system. These will serve as sample criteria for the adequacy of the system in achieving its goals. However, criteria need to be established for all three principal approaches to review, particularly those which can be applied to profiles or aggregate data and those for record review. Valid clinical criteria already exist in several programs.

An important issue related to the quality of dental care is underutilization; not all persons who need dental care are receiving it. Although many of the systems reviewed did look at this aspect of quality, only those that operate in highly defined populations could adequately deal with the problem. Most systems concentrate on the users of services and do not address those who are not. Efforts should be made to obtain utilization data whenever possible through dental prepayment administration, Medicaid programs, etc. The total eligible population in an area can be identified, and those who obtain services can be compared to those who do not.

Provisions should be made in a review system for testing the reliability and validity of criteria and standards.

Further Research Needs: A greater effort should be made to examine criteria development based on a topic-specific approach, particularly for record reviews. Increased utilization of nondentists will be necessary to conduct review to the extent possible in all areas where clinical judgments are not required.

The decisions relative to selecting a process of care require professional judgment. Efforts should be directed to developing and testing "branched" criteria for dentistry that reflect decision making. Branched criteria are structured to reflect the decision-making process in developing and carrying out a treatment plan. Depending on circumstances in each case, decisions are deemed acceptable or unacceptable.

Outcome review has several drawbacks, including the influence of outside factors such as patient compliance, systemic disease complications, and the fact that real outcomes may not be realized for many years. Emphasis should be given to the assessment of process and short-term outcome and to the examination of the capability of these approaches to truly reflect the quality of dental care and to identify basic problems in care.

PSRO law calls for the review of the necessity and appropriateness of care. Most dental quality assurance programs were not developed to comply with PSRO regulations. As a result, these two areas have not been addressed explicitly in current programs. Necessity and appropriateness of care should be priority items of criteria development, and the topic-specific approach should be considered a vehicle to carry this out.

The development of national sample criteria should be completed after aspects of care related to necessity, appropriateness and quality have been identified and systems and data sources to provide the desired information have been proven adequate.

Data Sources and Data Collection

Policy Considerations: Several disadvantages of clinical evaluation as a primary method of quality assurance have been documented. The cost of implementing a clinical evaluation program can be prohibitive because examinations must be performed by dentists. It also is difficult to use a random sample of cases since patient cooperation cannot be guaranteed. Clinical evaluations are also more likely to disturb existing patient-dentist relationships than are other methods that do not directly involve the patient. Because of these disadvantages and because of the extensive effort already expended in this area, the clinical evaluation approach to a quality assurance system should not be a priority. However, clinical examinations are valuable in determining the technical quality of care, and they should be reserved for those cases in which other methods of review cannot judge quality effectively.

The state of dental records needs examination, and the essential quality assessment components of the record need to be identified. If record audit will require changing the record keeping practices of the profession, consideration should be given, at least initially, to another existing data source, namely the claim form.

The costs associated with the profile type of review may be the most practical for first-level screening to de-

BEST COPY AVAILABLE

termine problems in ambulatory dental settings. The profile review does not require travel by dentists; data are collected and transmitted to a central point for processing.

Profiles should not be considered the sole method of review but should serve to identify treatments, conditions or providers that require in-depth review. Record review, pending identification of auditable records, should be used as the next level of review and should use explicit criteria to make review objective. If the question of quality is still not fully resolved, clinical examination may be necessary.

If several approaches to review are considered, integration of the information is required. Each approach may serve as a problem identifier for the others. Targeting review to identified problems provides an efficient way to determine the real causes of inappropriate care. Review can be targeted or focused on the identified problem areas, and other areas of dental care can be reviewed less frequently.

Further Research Needs: Data utilization or profile analysis based on encounter or claim forms should be one priority area in dental quality assurance research. The following factors should be considered:

1. Correlation of quantity information and the assessment of the process and outcome of care through other forms of review.

2. Identification by peers and PSRO of the most meaningful types of profile reports for assessing the quality of care.

3. Formulation of a minimum data set which can be gathered uniformly in all types of settings for the purposes of quality assurance. Data collected on the uniform claim form, approved by the American Dental Association, should be a starting point for such a data set. Other data that can provide assessments of outcome should particularly be stressed.

4. Any field test should build in comparable studies that use different approaches to the same cases so that the various methods of review will be validated.

Analysis and Peer Review

Policy Considerations. Documentation of decisions relative to profile analysis should be required. The report can serve as a feedback mechanism to enhance the understanding of review decisions.

Because of the desirability of review by peers, review committees should be established in those settings where peer review is not possible. In solo practices, review committees can be established through a consortium of solo practitioners.

Systems that are selected for implementation must provide methods to control for reviewer bias.

Feedback, Action and Appeals:

Policy Considerations. Provider acceptance of audit activities is a desirable and necessary goal. One means of gaining acceptance is to base the review system on provider input and to encourage provider participation in review activities. A provider is less likely to fear and oppose a system in which he is involved.

The current attitude of anger at criticism will be improved if it is possible for the provider to improve his care as a result of review. If educational programs are incorporated into the review system, review can become a learning experience for the provider rather than being simply a punitive monitoring technique. Many of the providers in the systems reviewed felt that engrained review activities would eliminate many of the malpractice actions health providers experience today. This could be another motivating factor for review participation.

Further Research Needs. The way in which the results of review are presented to the providers being reviewed should be examined further. It should be determined if it is more effective to demonstrate one dentist's practice patterns across many conditions or to compare his practice patterns with those of similar practitioners. The goal is to change aberrant behavior, and the way in which findings are presented may have a significant effect on obtaining desired behavior changes.

Follow-up

Further Research Needs. Monitoring provider behavior change is the least-developed facet of the follow-up methods reviewed. Research is needed to develop methods of gathering the data to check changes in provider behavior over time. Methods for mini-audits in noninstitutional settings also should be developed. Institution of valid procedures for follow-up audit of a small number of cases helps to eliminate subjective, one-on-one verification of behavior change.

Evaluation of the Review System

Policy Consideration. Although most of the programs regularly reviewed system components, in many cases the review process was neither structured nor documented. Efforts should be directed toward developing an ongoing system to review the components of the quality assurance program itself to ensure that the methods and procedures used are effective in achieving the program's goals.

Impact of Review

Policy Considerations. Because an extended time frame may be needed to identify changes in provider behavior patterns or in oral health status, long-range studies to evaluate the impact of a quality assurance program on provider behavior and oral health status should be planned at the outset of the program.

The complexities in examining the cost benefit relationship, make it necessary to look at review results over time. Aggregate the findings, and place some value on them. This value can then be related to costs of conducting review. Benefits of review in terms of improved efficiency in the use of dental resources and manpower should be weighed against the cost of review.

Further Research Needs. Development of appropriate measures of patient satisfaction is needed. The problem of biased respondents must be addressed to more fully assess the impact of quality assurances activities on patient attitudes.

There are standardized measures to review oral health

BEST COPY AVAILABLE

status, e.g., decayed, missing, filled teeth ratio, Oral Hygiene Index and Plaque Index. The feasibility of using these measures to evaluate the impact of quality assurance activities should be explored.

Indirect outcome measures should be developed such as the Index of Need or stage of care for assessing oral health status.

Field Test Protocols: Selection of models of quality assurance for field testing was accomplished through reviewing scores received using the Quality Assurance Model for Dentistry, comments on the systems from project consultants, and the systems' ability to address the research priorities identified in examining the state of the art. The field tests are intended to test not only the practicality of implementing a system of quality assurance, but also to test and examine some of the research recommendations identified in the study.

The objective of the current research is to identify models of quality assurance that are consistent with the PSRO format; thus, the proposed protocols focus primarily on appropriateness and necessity of dental treatment. Two of the systems examined in the study were selected for field testing. They were developed by:

University of Pennsylvania,
Department of Dental Care Systems,
School of Dental Medicine,
Leonard Davis Institute of Health Economics and
the National Health Care Management Center,
Philadelphia, Pennsylvania

Dr. Neal Demby and Dr. Murray Rosenthal
for the Sunset Park Family Health Center
Brooklyn, New York

A third program of quality assurance proposed for field testing is based on a model currently used in medicine by the Utah Professional Review Organization and is known as the Physician's Ambulatory Care Evaluation (PACE) program. The program is modified for dentistry.

The three projects would be monitored by a national advisory panel, comprised of practicing dentists, consumers and experts in quality assurance. It is hoped that through consistent evaluation of three field tests of dental quality assurance, the national advisory panel would be able to identify the strengths and weaknesses of each and to provide answers to many of the questions facing quality assurance in dentistry.

Field Test 1: The University of Pennsylvania staff has developed an overall resource management and quality assurance methodology that can be used in a variety of settings. The computer technology needed to implement the system has been created, as has a data set specifically designed for ambulatory dentistry. A modification of this system of dental assessment serves as one model that will be tested as a viable approach to review.

Objectives of the Project

1. To continue the development of a practical and effective method of quality assessment and quality assurance. The project has been designed to test and modify as necessary the system of quality review developed at the University of Pennsylvania by the Department of Dental Care Systems.

2. To further develop profile or pattern analysis as a viable, cost-effective method of review.

3. To evaluate the proposed quality assurance system in terms of effectiveness, impact of practitioners and practice structures and cost of operations.

4. To propose more widespread applications of the system to various practice, quality assurance system, and payment mechanism structures. Included in these recommendations would be the adaptations or modifications necessary to make the system applicable in these various settings.

Project Description. This field test proposes that a three-tiered system of quality review based on an adaptation of the University of Pennsylvania system be instituted in Worcester, Massachusetts under the administration of the Central Massachusetts Health Care Foundation (CMHCF) as a potential prototype for future large-scale review systems.

First Level: Profile or pattern analysis. Encounter data from dental offices in the Worcester, Massachusetts area will be analyzed by project computer staff through comparison of practice profiles.

Approximately 40 practitioners will participate through submission of encounter data on the care of approximately 300 patients each. Profiles, together with written commentary on their possible or probable significance, will be forwarded to a Dental Quality of Care Committee (comprised of dentists in the Worcester area) for review and further action.

Second Level: Focused nondentist review through data abstracted from selected dental charts. Based on the most plausible interpretation of profiles, the project computer staff will generate reports that will form the basis of a targeted or focused second level of review. These reports will identify specific practices, practitioners, and patient charts, and will explicitly specify what types of information a nondentist reviewer will abstract from the records. The Dental Quality of Care Committee will help define the types of information that the auditor will abstract.

In these reports, records will be selected in response to specific diagnoses, treatments, outcomes or patterns of care that are suspected to be problem areas. The auditor will thus have specified charts to audit for patients who have the same set of conditions in "reference" practices and for practices in which problem areas are suspected. The reference practices would be the ones that profile analysis suggests are delivering care at an above average level of quality.

The results of the audit data from the nondentist assessor will be forwarded to the Dental Quality of Care Committee for review and further action.

Third Level: "Peer review" by chart audit and/or direct clinical examination. When the Dental Quality of Care Committee is unable to make judgments about relative quality, or has insufficient information upon

BEST COPY AVAILABLE

which to formulate a quality judgment, members of the committee will act as assessors to audit dental charts and perform direct clinical examinations.

As to the second level review, the assessors will compare reference practices and practitioners with those that are suspected as being aberrant. Thus in none of the three levels of review is the assessment of general or diffuse. The profile is used to identify a specific suspected problem area, and the second and third levels gather information to permit the Dental Quality of Care Committee to determine if, in fact, a problem of poor quality exists. The technique of comparison of practitioners at different points in a range of performance is used.

Field Test 2: A protocol has been developed to test a second quality assurance system. The system, which has been operating for over five years at the Sunset Park Family Health Center in Brooklyn, New York, was developed jointly there by Drs. Neal Demby and Murray Rosenthal.

The proposed field test involves implementation of the management information system (MIS) and clinical examination portions of the Sunset Park system in the private practice solo and group offices of 30 general dentists in a rural area and 30 in an urban area of the same state.

Objectives of the Project

1. Test the effectiveness of the Sunset Park system in effecting change in practitioner behavior and improving both the quality of dental care provided and the oral health status of patients.
2. Test the feasibility of implementing this or a similar system in the private sector.

Project Description. In the initial data collection phase, a data abstractor will abstract encounter information for approximately 30 patients of each participating dentist. The patients will be selected from those who have received continuous care from the dentist for the previous five-year period. Clinical examinations of the same patients will be conducted at the participants' offices by two dentists, one from the local dental society's Peer Review Committee. The examination will also include a review of the record, radiographs and study models to determine the necessity of care and the appropriateness of the treatment plan.

Outcome of care as determined by the clinical evaluation will be compared to the process of care as determined by the patient and provider profiles developed from the encounter data which demonstrates service rates and treatment patterns. Through this comparison of cases, a correlation of process of care and outcome of care can be considered. Further, the validity of profiles as a method of assessing quality of care can be examined by correlating the results of review using indirect measures and the results of review using direct examination of the patient.

Each participating dentist will receive immediate feedback on this initial test and will have an opportunity to relate the process of care he has provided over five years to the current oral health status of the patients. In order to examine the impact of the system on dentist behavior and quality of care, encounter data will be collected for an additional 18 months on the initial sample of patients plus a sample of new patients.

The participating dentists will receive monthly computer-generated reports on the care they have rendered. Group statistics will also be sent to the peer review committees. This committee is then responsible for analysis, action and follow-up. At the end of the 18-month data collection period, a second series of clinical examinations will be performed.

Analysis of the results of the field test will focus on the impact of the system on the quality of care and on the cost of implementing the system. Other important aspects of the field test will be the comparison of the results of measuring the process of care to those of measuring the outcome of care, testing the validity of using profile data as a source of quality information, and testing the feasibility of expanding the role of component and constituent dental society peer review committees to include ongoing quality assurance activities.

Field Test 3: The claim form is a principal data source for third party review and has proven to be an adequate data source for screening purposes in medical care evaluation. For several years, the Physician Ambulatory Care Evaluation (PACE) program has used claims data and an advanced automated system for utilization and quality review purposes. Because of its success in the medical sphere, the PACE system has been selected for exploration as a model for ambulatory dental care evaluation. The PACE system is of particular interest because it is consistent with the intent of PSRO, the suggestions of project consultants who are in private practice and the recommendations of this study.

Most existing dental claims processing review systems focus primarily on utilization, fraud and abuse detection and benefit coverage. The PACE methodology, however, applies a more sophisticated computerized system of review which uses criteria for care developed by expert medical specialists to evaluate appropriateness of treatment provided as an aspect of quality. A physician's care that repeatedly varies from these peer expectations is examined more closely.

An essential feature of the PACE system is that it controls for claims form limitation as a data source by focusing on patterns of care rather than individual exceptions. Screening criteria are designed to accept a wide range of clinical practice and circumstances and to consider many variables, including procedures, types of patients, provider attributes and treatment time. The PACE system not only considers these variables as they appear on an individual claim form, but it also utilizes the memory function of the computer to look backward and flag forward a predetermined length of time to evaluate an entire sequence of treatment.

PACE criteria may be classified into five types:

1. required service or therapy,

BEST COPY AVAILABLE

2. contraindicated service.

3. prerequisite history needed to justify the service or therapy.

4. utilization limit for service or therapy.

5. untoward symptoms during therapy.

Adaptation of the PACE System to Dentistry. Because automated claims-based review of quality using the PACE logic is a new concept in dentistry, the model will be developed and implemented in two phases.

The first phase will address the issue of whether functional screening criteria can be developed to evaluate the quality and appropriateness of dental care using claims data. If functional criteria can be identified and the criteria prove sensitive to claims data, the second phase of the project will be to integrate the model into one or more existing claims processing systems and test the cost benefit of various methods of selecting claims for posttreatment screening. The purpose of the testing will be to identify criteria and a sampling methodology that focuses on problem cases, the product of which will be a more efficient, objective device for selecting cases for in-depth analysis.

Phase I

Goals and Objectives. The overall goal of phase I is to develop a theoretical model for quality review using dental claims data. This larger goal may be broken into seven objectives.

Objective 1. Develop screening criteria for automated quality evaluation of dental care using the PACE logic.

Objective 2. Identify appropriate data sources.

Objective 3. Program criteria into a software package and test them.

Objective 4. Review test results to determine if PACE logic is functional for dental quality review, and make indicated criteria revisions.

Objective 5. For each criterion, determine what, if any, additional information is needed to make treatment recommendations, make hypothetical treatment recommendations, and compare the results with actual recommendations for care.

Objective 6. Develop additional guidelines for use by nondentists in manually selecting exceptions and gathering information for peer review.

Objective 7. Make recommendations for testing the model in phase II.

Project Description. In establishing a set of criteria for use in automated quality review, a panel of practitioners will be asked to keep two considerations in mind:

1. Does the information provided by the criterion clearly indicate appropriate practice?

2. If the information is not a clear indicator, what additional information is needed?

Actual claims data will then be screened against the criteria, and all exceptions to the criteria will be examined. In determining if a criterion is a sensitive indicator, a committee will consider the volume of exceptions for each criterion, the significance of the identified problem on oral health, how well the screening process results reflect the quality of treatment, the contribution of the system to existing review mechanisms and whether aberrant behavior identified in the system could be altered. The system will be considered applicable if the data generated would be used to alter aberrant behavior.

Another major objective will be to determine if there are any patterns of exceptions so that different methods of sampling claims for retrospective automated review can be identified which will efficiently focus on the problems (i.e., by cost, by services, by provider).

Also, decisions made via computerized screening review will be compared to actual decisions made via routine pretreatment review to identify areas which may be more efficiently examined through the PACE type of review.

Phase II

Phase II will be used:

1. to identify the most cost-efficient application of the model to pretreatment review.

2. to identify one or more sampling methodologies for selecting claims for retrospective review.

3. to determine the impact of the system on practitioner behavior.

These will be accomplished by running the project on a much larger data base on an ongoing basis. Exceptions will be reviewed by a peer committee, education and actions for problems identified will be implemented. At the same time, comparisons of the volume of real problems identified and costs of identifying problems will be compared among the various sampling methods tested.

Finally, the three field tests proposed use profile analysis as a principal mechanism for review.

The profile based method as an approach to review was chosen to be field tested for two reasons: its anticipated cost-effectiveness and the availability of a uniform data source. Because dental researchers have found that patient records provide little more information than claim forms, testing a detailed record examination system did not seem advisable at this time.

However, the project staff and Care Consultant Committee did feel that record review, particularly as a second level review, is important and needs exploration. The most comprehensive approach developed to date is that proposed by Dr. Seymour Rotstacher, who identified a topic-specific approach to record audit using peer-developed, explicit measures based on the medical care evaluation (MCE) study model used in the hospital setting, and further examination of this approach in ambulatory settings is recommended. Dr. Rotstacher suggests these areas to study:

1. Workup—was the workup appropriate?
   a. History—What constitutes the necessary information that should be documented in the patient history before treatment?
   b. Examination—What should be noted in the examination for the patient's condition?
   c. Laboratory—What laboratory test findings are needed before treatment?
2. Elements Essential to Management—What items

BEST COPY AVAILABLE

of management are essential for treatment of the condition?

3. Complications—What complications might occur frequently and if found, should be reviewed?

4. Condition at Discharge—What is the optimal condition at discharge? (This may include patient instruction.)

All these field tests will be fully developed and funding will be sought to carry them out.

1. White, K.L., et al. *Ambulatory Care Quality Assurance Project*. Lafayette, California: Health Care Management Systems, Inc., 1976.
2. Hoffmann, J.J. Quality Assurance in Dentistry: A Perspective, unpublished paper, May 1977.
3. Schoenfeld, H.K. Evaluation of the Quality of Oral Care Systems, in Brown, W. (ed.) *Oral Health, Dentistry and the American Public*. University of Oklahoma Press, 1974.
4. Weinstein, P., Milgrom, P., Ratener, P., Read, W., and Morrison, K. Quality and Perceived Usefulness and Utilization of Continuing Education. *J Dent Res* 56A 141, 1977.
5. Brook, R.H., Williams, K.N., and Avery, A.D. Quality Assurance Today and Tomorrow: Forecast for the Future. *Annals of Internal Medicine* 85:809, 1976.
6. Bailit, H.L. Quality of Dental Care: Development of Standards. *JADA* 89:842, 1974.

RESOLUTIONS

This report is informational in nature and no resolutions are presented.

Mr. **Rogers.** Would you let us know what ADA is doing to insist that the dental schools carry out the thinking of the dentists of the Nation?

Thank you so much for being here.

Excuse me; Dr. Carter.

Mr. **Carter.** What percentage of your dental X-rays are of poor quality?

Dr. **Goepp.** We talked to this issue earlier, and the figures, for example, two-thirds, three-fourths, were thrown out. I think from my own personal experience, those figures are a little bit high; in fact, considerably high.

In addition, we must realize a patient cannot always cooperate, so one does not achieve what could be considered an ideal diagnostic film. Nonetheless, the film does provide the necessary information to take care of the patient.

In other words, if there is a water spot on a film, you realize that is not meeting the standards of an ideal film. In the interests of radiation safety, some of these people who espouse such rigid standards of idealism have to be checked because we should not reexamine a patient because there is a water spot on the film. That is unnecessary exposure.

Mr. **Carter.** In testing for certification of dental assistants, are radiological techniques and safety covered?

Dr. **Goepp.** Yes, sir.

Mr. **Carter.** Have there been any new developments in dental X-ray equipment to reduce the need to retake X-rays and to improve their quality?

Dr. **Goepp.** Yes, there have been helpful techniques in film positions, and alinement devices which reduce the number of retakes required.

Mr. **Carter.** To what extent are the dental auxiliaries who are taking X-rays tested and given certification for the use of X-ray equipment?

Dr. **Goepp.** As part of the education of dental assistants and dental hygienists, they have courses and knowledge given to them in both X-ray techniques and radiation safety, radiation biology, and radiation physics.

Mr. **Rogers.** How many States have testing and certification programs?

Dr. **Goepp.** I believe at this time there are two states, California and Florida, which have a certification program. Florida, I think, just implemented such a program very recently. Instead of licensure, which was talked about earlier, a certification, a certification

BEST COPY AVAILABLE

of continuing education, a certification of basic training, which already exists and which the ADA has promulgated as a standard, these people should have a training and such things already exist.

Continuing education is something that the professions are all working with now, and it is perfectly logical to see the renewal of radiologic knowledge would be part of continuing education. The certification that one participates in continuing education is a subject of State board licensure examiners who are developing this as a renewal of license.

So these activities are going on right now.

Mr. CARTER. Do you feel any controversy exists about the hazard or risk levels produced by dental X-rays?

Dr. GOEPP. Yes, there is some controversy. The reason for this is we are dealing with knowledge that is incompletely known. We have developed, in particular, low-level problems in our ancillary statement, but there are some voids in knowledge, and so there is controversy among people of equal expertise. It is not a matter of conflict between "know its" and the "know it nots."

Mr. CARTER. There are many different subject areas in dental education——

Dr. GOEPP. What was the first part of the question?

Mr. CARTER. Do many subject areas in dental education cover the use of X-rays?

Dr. GOEPP. Yes. We touched on this earlier. There is a formal recognition description of radiology courses, but because radiology is important in many treatment methods in dentistry, almost all of them, there is radiologic training and knowledge encountered in these other areas. So in oral surgery, while the students may be on an oral surgery service and so identified formally, they are seeing practical experience and gaining knowledge in the use of radiology too.

So it permeates the entire clinical setting of teaching in a dental school.

Mr. CARTER. Thank you, Mr. Chairman.

Mr. ROGERS. I think, if you don't mind, we would like you to critique the Pennsylvania Blue Shield study which indicated that two-thirds of the films were inadequate as a basis for determining the efficacy of proposed treatment plans.

I think, as I understand what they are saying, it says they are not adequate to be able to determine a course of treatment. That may be misinterpreted. So if you would look at the study for us and give us a critique, I think it would be helpful for the committee.

Dr. GOEPP. I thank you for that. In fact, that is a personal pleasure to do.

[The following letter was received for the record:]

THE UNIVERSITY OF CHICAGO HOSPITALS AND CLINICS
WALTER G. ZOLLER MEMORIAL DENTAL CLINIC
950 EAST 59TH STREET
CHICAGO · ILLINOIS 60637
(312) 947-6051

Office of the Director

August 10, 1978

To: The Honorable Congressman Rodgers, Chairman, Subcommittee on Health and The Environment of the Committee on Interstate and Foreign Commerce

From: Robert A. Goepp, D.D.S., Ph.D., Consultant, American Dental Association

Re: Request by Chairman Rodgers of a critique by Dr. Goepp of the "Pennsylvania Blue Shield Study" as per page 86, lines 1561 to 1572 of transcript HIF194040.

Dear Chairman Rodgers:

The study at issue here is:
A Study to Develop a Rating System and Evaluate Dental Radiographs Submitted to a Third Party Carrier.
By R. W. Beideman, O. N. Johnson and R. W. Alcox, J. Amer. Dental Assoc. 93, 1010 to 1013, November 1976.

Since I had no foreknowledge of this citation to your Committee, prior to my appearance, I attempted to place in time this study following your reference to it. I mistakenly associated with another event and said that I thought this paper was at least six years past. Actually, this paper is two years past. However, this is the paper which I thought was being cited. I did recall, during the testimony, that my original impression of this paper was that it had little scientific merit. My present restudy of this paper leaves me with the same conclusion as will become evident in my analysis of this study.

This paper is not mentioned or cited in Dr. Reiskin's prepared statement which I did have the opportunity to read before my appearance. Apparently this citation occurred in the nonprepared testimony. I have not seen that transcript, but if this citation was used to support a claim that there was unnecessary radiation hazard to dental patients, or that dentists are inadequately trained in radiology, the use of this citation is something less than a sincere and straightforward presentation to elected representatives of our congress.

I have placed here a copy of the table which summarizes the data of this study.

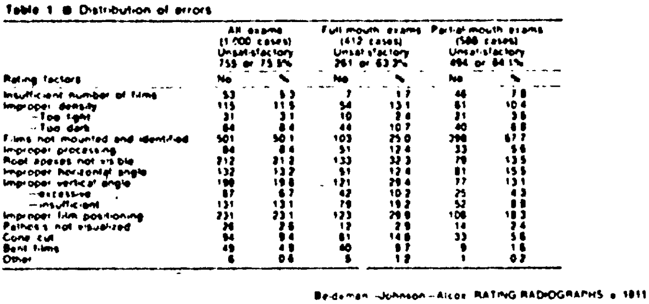


Table 1 ■ Distribution of errors

Rating factors	All exams (1,000 cases) Unsatisfactory 755 or 75.5% No.	%	Full mouth exams (412 cases) Unsatisfactory 261 or 63.3% No.	%	Partial mouth exams (588 cases) Unsatisfactory 494 or 84.1% No.	%
Insufficient number of films	53	5.3	7	1.7	46	7.8
Improper density	115	11.5	54	13.1	61	10.4
—Too light	31	3.1	10	2.4	21	3.6
—Too dark	84	8.4	44	10.7	40	6.8
Films not mounted and identified	501	50.1	103	25.0	398	67.7
Improper processing	84	8.4	51	12.4	33	5.6
Root apexes not visible	212	21.2	133	32.3	79	13.5
Improper horizontal angle	132	13.2	51	12.4	81	13.8
Improper vertical angle	198	19.8	121	29.4	77	13.1
—excessive	67	6.7	42	10.2	25	4.3
—insufficient	131	13.1	79	19.2	52	8.8
Improper film positioning	231	23.1	123	29.9	108	18.3
Pathosis not visualized	26	2.6	12	2.9	14	2.4
Cone cut	94	9.4	61	14.8	33	5.6
Bent films	49	4.9	40	9.7	9	1.5
Other	6	0.6	5	1.2	1	0.2

Biederman—Johnson—Alcox RATING RADIOGRAPHS • 1971

This table shows that 75.5% of cases examined were considered unsatisfactory or contained errors. By far, the most common error - 50% of errors - more than twice as much as any other error, was that films were not mounted nor identified. This means that the small dental films were not placed in cardboard or plastic holders. These holders have a definite pattern in the placement of each film, and the holder contains the patient's name, since there is no room on the film to place patient identification. Dentists mount such films in holders for their own convenience in viewing the films. Why so many dentists choose not to offer this convenience to the insurance company, although it is asked for, is not clear, but more likely it is based on the quality of the relationship between dentist and insurance company. But this so-called error has absolutely nothing to do with any radiation hazard to patients, nor is it any indica-

tion of the amount or quality of instruction in radiology; nor is it a measure of the amount of radiologic expertise possessed by a dentist. The weaknesses in this study about the remaining 38% of errors are not as obvious as the mounting error, but the weaknesses are detectable. The next highest incidence of error was reported to be improper film positioning, 23%. The term "improper film positioning" is not clearly explained in this paper. This may mean: what parts of what teeth are represented on which particular film. There is a difference of opinion among dentists as to exactly what area should be covered by each film.

The error called "improper vertical angle" should be defined in this paper since there are two different technics relative to vertical angle taught in different dental schools: the parallel technic and the bisecting angle technic. It is well-known that the advocates of the parallel technic consider the bisecting angle technic an error, and in my opinion, the parallel technic is better, but the difference is not important as a cause of radiation hazard or faulty diagnosis.

Bent films are mentioned as an error. I do not advocate bending of films, but there are radiology teachers and textbooks which advise bending of films to facilitate placing of the film in the mouth and for patient comfort.

The reason for such apparent confusion and the major weakness of this paper is given in the paper itself, pages 1012 and 1013. The pertinent part is excerpted here:

> To test interexaminer reliability, a member of the Bureau of Radiological Health (examiner no. 1) rated 34 case submissions consisting of 20 full mouth and 14 partial-mouth series, which were independently reviewed by the principal author (examiner no. 2). There was total agreement on 19 of the 34 case submissions (56%). For each of the remaining 15 case submissions, there were one to three areas of disagreement. Table 2 shows the frequency distribution of differences by specific error.

> The 19 cases of total agreement occurred with no prior discussion between examiners on definition of errors. For instance, incorrect horizontal angle was defined by examiner no. 1 as any overlap of tooth images. Examiner no. 2 defined incorrect horizontal angle as an overlapping of tooth images great enough to obscure dentin. Advance collaboration on definition of terms would lead to increased interexaminer agreement. This would be essential if several people were reviewing case submissions.

The text of this excerpt demonstrates that there can be almost 50% disagreement among professed experts as to what constitutes ideal characteristics of a dental x-ray examination or, conversely, what errors are in such examinations. As the paper states, with prior agreement among reviewers, the deviation is reduced to more tolerable levels. However, in the light of the diversity of opinion about standards of quality for an exposed dental x-ray film, even demonstrated in this paper, the arbitrary standards used in this paper cannot support a claim that dental radiology films generally contain 75% errors.

At this, it comes to my mind that the above described diversity of opinion which probably arises from the amateurish experience and knowledge of many dental radiology teachers, whom I suspect have little more training in radiology than that received when they were a dental student, is a point that I was trying to make in my testimony plea, HIF194040 p. 72, lines 1301 to 1309, and our prepared statement p.4, item C(1)a, for help in upgrading the teaching of dental radiology.

One of the recommendations found in this paper, p. 1013, is excerpted here:

> —All rejected radiographs should be returned with a request for adequate films and an explanation of why the case submission was rejected. The rating form with appropriate errors checked could be used for this purpose.

This is an example of the mentality - pursuit of irrelevant ideals - to which I alluded in my testimony, HIF194040, p.67, lines 1200 to 1204, which leads to re-exposure, an unnecessary exposure to radiation. A far better standard for judgement of film quality is: does the film give the information which is needed to answer the original indicated need for an x-ray examination?

May I also take this opportunity to clarify a statement in my testimony, HIF194040, p. 67, lines 1204 to 1206. My statement was not clear and you, Mr. Chairman, by your response, thought it related to radiation injury. Rather, by "how come we are not all much sicker than we are," I meant that, if 75% of dental x-ray films were with errors, we would all have many wrong teeth filled, wrong teeth extracted, and suffer significantly from undiagnosed other oral diseases.

Sincerely and Respectfully Submitted,

Robert A. Goepp, D.D.S., Ph.D.
Consultant, American Dental Association

Mr. ROGERS. We are grateful to you. Your assistance to the committee is most appreciated. Thank you for your presence.

Our next and last witnesses will be on behalf of the American Hospital Association. Dr. Leo J. Gehrig, who is senior vice president, American Hospital Association; George Caldwell, who is president of the Greater Southeast Community Hospital Foundation; and Dr. Louis Wener, chief of the Department of Radiology of the Greater Southeast Community Hospital Foundation.

We welcome each of you gentlemen to the committee. We are pleased to have you with us.

Your statements will be made part of the record, and you may proceed as you desire.

STATEMENT OF LEO J. GEHRIG, M.D., SENIOR VICE PRESIDENT, AMERICAN HOSPITAL ASSOCIATION, ACCOMPANIED BY GEORGE CALDWELL AND LOUIS WENER, M.D., ON BEHALF OF AMERICAN HOSPITAL ASSOCIATION

Dr. GEHRIG. Thank you, Mr. Chairman.

I am Dr. Gehrig, senior vice president of the American Hospital Association. As the committee chairman knows, our association represents most of the hospitals in the country and some 27,000 personal members. I would say that we appreciate this opportunity to participate in your oversight hearing.

I have submitted a full statement for the record and will not repeat it. I would like to highlight a few of the points [see p. 675].

Mr. Chairman, in this oversight situation, if you would permit me a personal prerogative.

Mr. ROGERS. Certainly.

Dr. GEHRIG. There are lots of types of oversight, and I think personally and on behalf of the many, many hospitals and their administrators in this country, I would like to set our feelings in the record, if possible, with regard to a statement that you made in the very recent past.

We have, on occasion, found ourselves on different sides of the table, but many, many more times we have worked very constructively with you. When you announced that next year you would not be returning to this Congress, I want you to know we feel very strongly that we in the hospital field, the other providers, the Congress and our country have a loss because of the leadership and ability you have demonstrated.

I say this for no personal reason except an honest expression, and we wish you the best in everything you attempt to do in the future.

Mr. ROGERS. That is very kind. Thank you.

Dr. GEHRIG. With regard to this hearing—and I appreciate you permitting me to make that comment—our statement points up activities which our association is presently pursuing with the hospitals across the countries in the area of health promotion.

While this is a broad area—and I shan't go into it—one of the areas of concern is increasing among our patients in the communities with which we deal; an awareness of the hazards of X-ray and really positive actions that are also possible by patients in avoiding such hazards.

For the purposes of the committee—and I shan't go into it—we have available some of the materials for your staff that we have been working on in this area.

Mr. ROGERS. Fine.

Dr. GEHRIG. Second, in my statement there is an area which points up an activity that AHA began in 1951 along with the American College of Surgeons, the American College of Physicians, the American Medical Association, and the Canadian Medical Association—the cofounding of the Joint Commission on the Accreditation of Hospitals. This is an exceedingly important area, and while its examination of hospital activities run across the breadth of these activities, one of the most important is in the area of radiology.

We have provided to the staff specific information for their perusal in terms of the inspections that are made. But, as you can see, the accreditation manual and its review of hospital activities is much broader, and we will provide that to them also.

This program of the joint commission and its surveys which, in addition to its own standards, mandates the application of recommendations by the National Council on Radiation Protection and Measurement, is but a part of the inspection that is made of hospital radiological departments. I think those who have testified here today and before today have pointed out that local State and Federal agencies, as well as voluntary groups, are involved in this type of activity. And while these important reviews deal largely with external examinations, they build upon internal professional and management activities of quality control, radiation safety, medical audit, educational programs, and administrative reviews. These internal actions involve the professional staff, the administration, and the hospital's board of trustees.

Finally, Mr. Chairman, in my testimony I point up that the relatively closely monitored activity of hospitals is, in fact, undergoing some of the very drastic changes we see across the breadth of medicine in terms of advances. We are seeing the development of such things as CAT scanners and monitoring devices as well as exposure controls and automation in both the taking and developing of films.

We are seeing at the same time changes in diagnostic patterns. There is one area I know you will want to pursue—the gentlemen with me who are on the firing line and very knowledgeable—that is the matter of routine X-rays.

If I could personally digress—and I am sure Dr. Carter would join me in this observation—it was almost 30 years ago that I directed the chest disease activity for the territory of Alaska on assignment from the Public Health Service. It was at a time when the number one health problem in Alaska was TB. We recommended very strongly anyone in the hospital who had not been X-rayed in the last year be X-rayed.

We ran around the country rather frantically with mass surveys, trying to find this killer. As a matter of fact, we were doing it in an environment that was rather unique, because at that same time in Minnesota, the advances in treating TB had rendered classes of students in high school literally free of tuberculin reaction.

In Minnesota they could use skin testing. In Alaska, our high school students were almost 100-percent reactors to tuberculin testing, so we had to use X-rays.

What happened then is what we have seen in a broad way across the country. In Alaska, you can't find TB as a primary cause of death.

We see an evolution that I think institutional medicine, public health and the private providers are all going through.

Finally, in terms of changes that have been giving us a great deal of problems, as we see these technological advances, we are also seeing advances that relate to costs.

I think radiology represents one of those changing areas. I point to that fact in our testimony. You know, it is not uncommon in hospitals to see part- or full-time consultation with radiation physicists, individuals who, 25 years ago, were rather rare in the clinical edge of radiation. My statement deals with these areas.

Much more to your interest are the two gentlemen with me, Mr. George Caldwell, who is the president of this Greater Southeastern Community Hospital Foundation, and the hospital chief of radiology, Dr. Louis Wener. We would be delighted to be as responsive as we can to any of the questions you may have.

[Testimony resumes on p. 679.]

[Dr. Gehrig's prepared statement follows:]

AMERICAN HOSPITAL ASSOCIATION
444 NORTH CAPITOL STREET, N.W., SUITE 500, WASHINGTON, D.C. 20001 TELEPHONE 202-638-1100
WASHINGTON OFFICE

STATEMENT OF THE AMERICAN HOSPITAL ASSOCIATION
TO THE
SUBCOMMITTEE ON HEALTH AND THE ENVIRONMENT
OF THE
COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE
OVERSIGHT HEARINGS ON MEDICAL AND
DENTAL DIAGNOSTIC X RAYS

July 13, 1978

Mr. Chairman, I am Leo J. Gehrig, M.D., Senior Vice President of the American Hospital Association. With me today are George Caldwell, President of the Greater Southeast Community Hospital Foundation in Washington, D.C., and Louis Wener, M.D., Chief of the Department of Radiology of the same hospital. Our Association represents over 6,400 health care institutions, including most of the hospitals in the country; extended and long-term care institutions; mental health facilities; and hospital schools of nursing, and over 27,000 personal members. We are pleased to have this opportunity to participate in these oversight hearings on the diagnostic use of medical and dental X rays.

Health Promotion

The American Hospital Association shares the desire of this Committee to assure safe, reliable, and appropriate health care services, including diagnostic X-ray services in the hospital setting. With regard to such services, I would like to provide the Committee with a brief overview of the work of our AHA Center for Health Promotion. This Center was established to build upon the Association's existing programs in patient education, consumer health education, and employee health. Through the activities of the Center, the AHA has placed major emphasis on the responsibility of hospitals to develop even more energetic policies and procedures to keep people healthy, to maintain higher levels of health and well-being, and to educate individuals and employers concerning the prevention and treatment of illness.

Currently, the Center is developing extensive patient education materials on diabetes, hypertension, respiratory disease, and arthritis, as well as materials and programs on nutrition and medical information. These activities are being funded in part by a grant from the Department of Health, Education, and Welfare. Recent AHA consumer health information programs have focused on such subjects as child immunization, stress management, and stop-smoking clinics.

As part of these current activities, the Center for Health Promotion has been in contact with the Bureau of Radiological Health of the Food and Drug Administration, and plans are being developed to promote the Bureau's new consumer and patient education materials to the Association's membership. Five of the American Hospital Association's personal membership societies will publicize the forthcoming materials to more than 6,000 individuals responsible for hospital programs in education, public relations, nursing, and social work, and for volunteers, and auxiliaries. Several groups will provide their members with educational materials such as free sample posters that warn: "Pregnant or think you might be? Tell your doctor before getting an X ray or prescription!" Further, these groups will promote the availability and encourage use of an X-ray/vaccination record card, various informational booklets, brochures, reprints, and a new slide-type program offering consumer information about X rays. Hospitals with videotape capability for educating patients, visitors, and community groups will be encouraged to use the FDA informational program as part of their own health promotion efforts.

The radiological health education program also will be promoted to hospitals through regular AHA publications and workshops. Where appropriate, the Association will provide information about materials available from the Bureau of Radiological Health and will include information in its consumer-directed, subscription radio series, "To Your Health."

Finally, Association members will be given information about the FDA field staff who are available to assist local hospitals in developing more extensive programs on radiologic health for the general public as well as for health personnel.

Standards and Accreditation

While education is a major function of the American Hospital Association, we also recognize and actively support the Joint Commission on Accreditation of Hospitals (JCAH) and its role in setting standards.

The Association's involvement in the voluntary hospital accreditation program of the JCAH has resulted in stringent standards governing user maintenance and testing of all hospital equipment. These JCAH standards require that all performance and use specifications for medical equipment be regularly tested and verified. JCAH standards also mandate the application of recommendations by the National Council on Radiation Protection and Measurement, which include requirements for routine output measurements of radiation therapy equipment, and the regular application of major calibration procedures on all diagnostic radiologic equipment.

The JCAH standards also include extensive specifications for radiologists and technical personnel, physical areas used for X rays, safety rules, medical records, and policies and procedures governing hospital use of radiology services. Because the JCAH standards address virtually the entire spectrum of radiology services in the hospital setting, we are providing the Committee with a copy of these standards for informational purposes. In addition, inspections of radiologic equipment and services in hospitals are performed by local, state, and federal governmental agencies, as well as other voluntary organizations.

Medical Equipment

To assist hospitals in the development of comprehensive and effective equipment maintenance systems, the Association has presented numerous medical equipment management educational programs. Further, the AHA has taken a leadership role in the recent development of a program to aid hospitals in establishing responsive medical device defect recall and reporting systems. This will speed the removal of defective equipment from hospitals and enhance various national medical device hazard reporting systems. We believe that such efforts, and those of other professional organizations, will assist in assuring the reliable, safe, and effective performance of medical devices.

In response to the recent guidelines for "Radiation Protection Guidance to Federal Agencies for Diagnostic X Rays," as approved by the President, (Federal Register, Vol. 43, No. 22, Feb. 1, 1978, p. 4377), the AHA has developed an active liaison with the Bureau of Radiological Health to examine how these recommendations may be implemented cost effectively within the private sector. The development of a series of national educational programs on equipment quality assurance is now underway.

Professional and Administrative Activities

Physicians, hospital administrators, and hospital governing boards are involved in a variety of efforts to provide high quality radiology services with appropriate safeguards for the health of patients and employees.

In many hospitals, special committees have the responsibility of surveying the practices of ionizing radiation service areas to assure both patient and employee safety. The members of the committees represent physicians and the hospitals' administrative staffs, and submit either the minutes of their meetings or their recommendations to the chief administrative officers and the governing boards, thus assuring that the highest levels of administration and governance are involved in the monitoring and management of this important service.

Similarly, the professional staffs of hospitals, as well as Professional Standards Review Organizations, are involved in peer review activities and medical audits of radiologic services in a variety of diagnostic and therapeutic applications. These monitoring and educational activities are important to the safe and appropriate use of X-ray services.

Increasing Efficiency and Effectiveness of Radiology Services

Means are being devised to make radiology services more efficient and effective. For example, automatic exposure services are coupled with ionizing radiation equipment to control the intensity and duration of exposures, resulting in fewer units of exposure and fewer retakes. Another example of advances in radiological services is the use of CT scanners. Originally, scanners were thought to be useful only for analyzing or diagnosing brain conditions. However, such scanning is now proving valuable in diagnoses involving other areas of the body. Further, the scanning procedure is being substituted for traditional diagnostic procedures that were more invasive and traumatic to the patient and were accompanied by greater risk--for example pneumoencephalograms.

Today, most hospital medical staffs no longer require routine X rays for patients, a practice common in the past. For example, 30 years ago, many public health programs encouraged annual chest X rays. Changing patterns of disease and increasing concern about levels of X-ray exposure have resulted in discontinuance, or marked limitation, of such routine or survey use of X rays.

Radiation physicists as well as radiologists are serving in many larger hospital radiology departments. This improves (1) the evaluative and quality assurance programs, (2) continuing education directed at improving practice, and (3) proper scientific evaluation of radiation monitoring procedures.

Conclusion

Mr. Chairman, this concludes the American Hospital Association's formal statement. We will be pleased to respond to any questions you or other members of the subcommittee may have.

Mr. ROGERS. Thank you so much, Doctor. We appreciate the presence of each of you.

Dr. Carter.

Mr. CARTER. Thank you, Mr. Chairman.

It is just about as you said. Years ago chest X-rays were almost routine, and tuberculosis was rampant throughout the United States and also in Alaska. I know it was one of our No. 1 killers in the State of Kentucky. Perhaps our X-rays did cause some difficulty. We have to admit possibly they did. But at the same time, we practically eradicated tuberculosis; is that not correct?

Dr. GEHRIG. Certainly its incidence is way down.

Mr. CARTER. I was interested in how a CAT scanner can prevent the actual trauma. Do you remember the technique of giving a pneumoencephalogram?

Dr. GEHRIG. Yes, I do. And I am sure Dr. Wener is well familiar with it also.

Could you describe that, Doctor?

Dr. WENER. Yes, sir. Pneumoencephalography is an examination of the internal structure of the brain performed by the introduction of air into the spinal column, usually by spinal tap, with patient in upright position. Of course, the air would then rise from the spinal tap into the brain and outline the internal structures of the brain.

Mr. CARTER. It can be done just by spinal tap, but by going in at the base of the brain, I believe. It is one of the most difficult procedures; where after you insert the needle, you hit a bone.

Dr. WENER. Right.

Mr. CARTER. And then you inject the air. That really is a difficult and quite dangerous procedure.

Dr. WENER. Extremely.

Mr. CARTER. I would think that the CAT scanner would be more helpful and a lot safer even with the attendant radiation exposure. Do you think so?

Dr. WENER. Yes, sir, you are quite right. That examination, fortunately, has been virtually eliminated from the diagnostic armamentarium. I think we have done two of them in the past year that were obviously required. There was no way to get around what we needed to know, and the CAT scanner could not give us the information.

You are absolutely correct; it is certainly worth the risk of exposure.

Mr. CARTER. Does that air go into the fourth ventricle here at the base of the brain?

Dr. WENER. Fortunately, Dr. Carter, we don't have to——

Mr. CARTER. It goes in between?

Dr. WENER. Yes, sir, it goes into the fourth at that point. Fortunately, we can avoid these cisternal punctures you are doing by doing the lumbar puncture. Your assessment of the danger of that puncture, when necessary, is absolutely correct. It is probably understated.

Mr. CARTER. But I understand that you are educating your patients with placards stating that women should beware of X-ray procedures if they are pregnant.

Dr. GEHRIG. Yes, sir.

Mr. CARTER. And to beware of certain medicines if pregnant, and so on.

Let me congratulate you on what you are doing in this area.

Dr. GEHRIG. Could I mention one other thing that impressed me?

This really is a development of the Food and Drug Administration and their efforts, but we are cooperating with them and others in putting this out. That is, the patient portable X-ray record.

It is an effort to have available information concerning past X-rays and their application wherever possible so that substitution can be made on occasion.

Mr. CARTER. Yes. I think that is very fine.

I think we should have cards showing the number of millirads of radiation exposure we have had over a period of time if we want to try to avoid risks of developing cancer.

Thank you.

Mr. ROGERS. I think it is generally conceded that about two-thirds of all X-rays are given in hospitals. What do you see as the hospitals', the associations' role in curbing excess X-rays?

Dr. GEHRIG. No. 1. I think, very honestly, Mr. Chairman, the whole statement of unnecessary X-rays is such a broad one and it is an extremely difficult one to define. I think, first, as an association, some of the things that I have mentioned here already relate to that.

In other words, the encouragement of having X-ray records and the use of examinations that have been done prior to admission certainly avoiding the taking of unnecessary X-rays. Similarly, making the patient aware of the advantages of avoiding X-rays, is another method, but I think there are a host of other issues.

One is the quality of X-ray work being done and the number of retakes. In this area it would be helpful to your discussion, I think, if I could ask Mr. Caldwell and Dr. Wener to talk both from the point of view of what is happening in stitutions.

Mr. ROGERS. Mr. Caldwell.

Mr. CALDWELL. Thank you.

As president of a hospital, I am not as familiar technically as Dr. Wener, so I will avoid the technical matters.

I, however, do wander through the X-ray department every day, and there are yellow signs—-

Mr. ROGERS. Shielded, I hope.

Mr. CALDWELL. Shielded, indeed. There are yellow signs with black letters that say if you are pregnant, tell somebody. I am well satisfied, as is our board, that the necessary quality controls are in, calibration programs are looked at.

We have, indeed, a full-time person whose primary responsibility is quality assurance in that department.

In terms of exactly what we are doing and what we think is more and more becoming common practice in hospitals in terms of calibration of equipment and checking the processing, I think Dr. Wener is in a much better position to talk about it than I.

I would like to mention that there is a new accountability in this country on the part of boards of trustees as regards quality that has happened over the last 10 years and that accountability has not escaped our board.

Our board, as a matter of policy, has recently established certain guidelines as it relates to these professional departments in which we are required to produce for that board reports on the administrative as well as the professional aspects of the department quarterly to the board, and there is a reporting mechanism on these matters that is terribly important to the board and terribly important to me in terms of our accountability.

In terms of exactly what goes on as regards quality assurance in radiation exposure and the rest, I would like to defer to Dr. Wener.

Mr. ROGERS. Is your radiological department a moneymaker as such, or does it run in debt?

Mr. CALDWELL. It breaks even. We are principally reimbursed on a cost basis here. Our hospital is in the District of Columbia. Medicare/medicaid and Blue Cross, of course, are all cost contracts.

Mr. ROGERS. Is there any hospital effort to reduce procedures, radiological procedures?

Mr. CALDWELL. Indeed, there are efforts to reduce costs. As far as reducing procedures, Dr. Wener can speak to that better than I. As far as reducing costs, we have what we would expect modern management to have in terms of reporting systems and budgets, and we look monthly at man-hours per procedure, and we can tell you where that is.

Mr. ROGERS. If you have a particular number of X-ray procedures that are dramatically increased——

Mr. CALDWELL. We examine our mix.

Mr. ROGERS. To see why?

Mr. CALDWELL. You bet; indeed.

Mr. ROGERS. Then you advise the staff of the concern that you have?

Mr. CALDWELL. Yes, sir.

Mr. ROGERS. Does the hospital assume that responsibility?

Mr. CALDWELL. The management does assume the responsibility of examining that mix, and where there are variations in mix, we inquire from the proper body.

Mr. ROGERS. And then you will talk to the staff and have it brought to their attention?

Mr. CALDWELL. There are two mechanisms to do that. There is the joint conference committee between the medical staff and the board, and the board has its own quality assurance committee that would be interested in that kind of data. I think that is fairly common these days.

Mr. ROGERS. Thank you.

Dr. Wener.

Dr. WENER. I think if I may amplify ~~something~~ that was said earlier, it really becomes very critical when you are looking at numbers of exposures or numbers of procedures to recognize the danger in using the word "unnecessary." In fact, in looking through the testimony that was given to you yesterday by the ACR, the studies of Drs. Bell and Loop on the skull X-ray and its potential saving of money in this country and radiation exposures, on one examination, is pretty dramatic.

The important thing is whether or not the X-ray examination will, in fact, affect the course of therapy. To that end, one wants to do what one must to help the patient with the least risk to the patient, and I think probably the single biggest advance that we, along with others, have made recently has been the institution of quality assurance programs. This includes things such as making sure that there is linear calibration of the machines.

We have 10 rooms. All of these rooms are calibrated identically or as near identically as possible so that any given technologist could go from one room to the other and use the techniques that have been set down in our technical handbook and, in fact, produce satisfactory diagnostic images without the necessity for retakes.

One of the primary problems of unnecessary—excuse me; I am using the word again. One of the problems of retaking films comes from faulty processing. And in as short a time as this morning, our quality assurance technologist walked into my office and presented me with a homemade alarm that he has rigged that, for a cost of $50, will detect a variation of two degrees in the temperature of the developing solutions and audibly sound the alarm. This way we think that we can virtually eliminate processing errors for a simple $50 expenditure and thus greatly reduce the number of retakes because the processor drifts off.

Mr. **Rogers**. Has he patented that yet?

Dr. **Wener**. No, sir, I don't think he plans to.

Mr. **Rogers**. Maybe the AHA would help get that around.

Dr. **Wener**. I suspect it will be published. It is a rather ingenious and simple thing.

Mr. **Rogers**. Couldn't you put that in the magazine of the American Hospital Association as an interesting news story, even?

Dr. **Gehrig**. That is one way we can dedicate it to the public without a copyright.

Mr. **Rogers**. If he is willing to do it.

Dr. **Wener**. I am sure he will be willing to get it spread around.

Mr. **Rogers**. Let me ask this: You run the department for the hospital?

Dr. **Wener**. Yes.

Mr. **Rogers**. Do you work for the hospital?

Dr. **Wener**. Actually not. I am an independent contractor. I supply a professional service to the hospital.

Mr. **Rogers**. You then do not take—it wouldn't be possible, I presume, for you to take all the X-rays?

Dr. **Wener**. No, sir.

Mr. **Rogers**. You have technologists. Are they qualified, certified or licensed technologists?

Dr. **Wener**. They are certified.

Mr. **Rogers**. By whom?

Dr. **Wener**. By the American Registry of Radiologic Technologists, ARRT. This is a standard that our department has set and, I believe, conforms generally to the standards set across the country by hospital departments.

Mr. **Rogers**. What have you done for the hospital to suggest a reduction in the numbers of X-rays to be taken? Anything?

Dr. **Wener**. Other than to eliminate what we consider technical problems leading to excessive exposures, I would say to you that simply the presence of board certified, adequately trained radiologists and competent radiographers or technologists in the department. We believe that we do the amount of exposures necessary to properly care for our patients. I would like to believe that that is the proper amount.

Mr. **Rogers**. Let me ask you this: Suppose one of your doctors say, "Well, I need all this series." You, as a radiologist, may not agree with that.

What happens?

Dr. **Wener**. In that instance, we are very fortunate because we have a pretty fine working relationship with our referring staff. I think your point is extremely well taken. We are consultants to those physicians, and I have no hesitation to call up that physician and, indeed, do on many occasions and say, "What are you looking for?"

And if what he wants to find is something I think there is a better way to go after without risk, time and involvement of the patient, then we will suggest that.

I am happy to say our staff normally will go along with that.

Mr. **Rogers**. If they don't, what?

Dr. **Wener**. If they don't, it is still my decision.

Mr. **Rogers**. You can still refuse?

Dr. WENER. Absolutely.

Mr. ROGERS. Will it affect your income if you didn't go along with some of them?

Dr. WENER. To the extent I don't do a study, I won't get compensated for it.

Mr. ROGERS. If he doesn't refer his work to you?

Dr. WENER. If he doesn't, I am sure whatever portion of my income is derived from his work would probably suffer. But I don't know that we have ever really considered that.

Mr. ROGERS. We have just had testimony from a radiologist yesterday, and I am not sure he was hospital-based, which I think might make some difference, too.

He said up to one-third of his income has been affected because he gave the advice and when it was in error for the pictures to be taken and he would not agree to it professionally, he simply wouldn't do it, and those doctors then refused to use his services.

I presume that is human nature. I just wondered, and I presume that is a factor we should deal with. What I am trying to get at is, should there be a requirement that each X-ray procedure have the specific approval written on the form by the radiologist?

Dr. WENER. I think that practically would be virtually impossible to do.

Mr. ROGERS. Why?

Dr. WENER. I think that in the main, most routine requests, as Dr. Morgan stated, do go unchallenged. We have a requirement in our hospital, and the JCAH is becoming more stringent about this, we are looking toward more efficient ways of making sure that it is done; that adequate history be presented to the radiologist on the request slip.

I will tell you with some pride that if you use qualified radiographers and people who are really trained in the use of X-ray, those people who take the pictures—and they are the ones who primarily interact with the patients—that in our hospital it is not an infrequent occurrence for one of those radiographers to come up and say, Dr. Wener, I was talking to this lady and she says she doesn't really need this thing, and I was wondering if you would look into it.

Quite honestly, we will look into it, and very frequently the technologist is right; the patient has either had the incorrect examination ordered or something like that.

So we do have sort of a buffer. I think to require a radiologist to initial every request in a hospital such as ours that does 100,000 examinations a year in X-ray alone, I think you would find that almost an overwhelmingly impossible task.

Mr. ROGERS. Is the patient entitled to have the judgment of the radiologist made? He is paying for it.

Dr. WENER. He is paying for the radiologist's opinion and judgment, and you are quite right; the patient is entitled to that. We have set down some broad guidelines that our technologists and medical staff are aware of.

To that end, the patient is indirectly getting the benefit of that. I think that to expect a radiologist to evaluate and sanction patients really stems into the purview of the private physician who, hopefully, has made a judgment based on his relationship with the patient and asks for a radiological consultation.

Mr. ROGERS. Aren't you the consultant as far as the radiological phase of the patient's treatment is concerned?

Dr. WENER. Yes, sir. And as such, that is what I said to you; the final word on whether that study is done or not still rests with me or my staff.

Mr. ROGERS. It just seems to me there still is not the responsibility placed upon you for an accountability that gives to the patient the assurance that you, as a radiologist, have really made that judgment and determination as a consultant, because you then say, Well, the doctor called for these series and those are generally——

Dr. GEHRIG. Looking at it as a physician who is not a radiologist—and I have my boards in thoracic surgery—I felt I knew a little bit about that. I really think this is moving in the direction of an absolute. I think the majority of X-ray examinations that are done by conscientious physicians probably are well justified.

In the development of one's history and one's rationale for pursuing this type of diagnosis, quite a bit goes into it; a lot more than you can put on a small space of an X-ray request. I don't think there are that many abuses or that many concerns for a specialist consultation for, say, 80 percent or some such figure. I think there is an area in which many physicians have a doubt and use the radiologist appropriately as a consultant in a difficult decision.

I really think making that second guess on every X-ray that comes down the pike is another way for us to spend a lot of money with very little secondary assistance to patients.

Dr. WENER. Mr. Rogers, excuse me. Let me add one thing.

In our hospital—and I believe this is a trend—the medical staff has no routine radiographic orders. There is no order for a routine admission chest X-ray, nor is there an order for a routine preoperative chest X-ray. Each one of those films—and admittedly the vast majority of patients coming into the hospital and/or having surgery will get a chest X-ray—those orders have to be written and have to be written by the attending physician. So there is no blank that somebody stamps out that sort of shoves that patient in front of an X-ray beam. It is a decision made by the referring physician and tacitly sanctioned by the radiologist.

That, of course, is not true with a more risky examination; the so-called special studies.

Mr. ROGERS. What about skull X-rays?

Dr. WENER. Skull X-rays would fall into those categories that are requested by the attending physician, but there is no routine skull.

I might add, probably the greatest impetus to doing skull examinations comes from the patients, not from the doctors; the necessity for avoiding possible litigation. We have an extremely busy emergency room. We do a lot of skull X-rays. The reason we do them is because the doctors who order them feel they need them to protect themselves or the patients come in saying, I have just hit my head; I am on my way to my lawyers. Would you please X-ray my skull?

Mr. ROGERS. Do you use the Phillips high-yield criteria?

Dr. WENER. I am afraid I am not familiar with what you are talking about, sir.

Mr. ROGERS. This is where they say, I think they have reduced them to 7 now, haven't they? It was 10 to 7, I recall, at the University of Washington Hospital. They have shown if certain criteria are checked from the patient, unless some of those exist, there is no need for a skull exam.

Dr. WENER. You are talking about Dr. Bell's and Loop's study. I venture to say that probably that is not done routinely across the country, and I suspect it is not done in our institution as well.

Mr. ROGERS. Should it be?

Dr. WENER. Absolutely. Absolutely.

Mr. ROGERS. What could we do to get that done? What could the Hospital Association do; anything? Could accreditation request that?

Dr. GEHRIG. I am not sure this focuses. There is really an area we haven't touched on that Dr. Wener is involved in and others like him that is extremely important. This really grows out of a PSRO quality assurance type of program. I think, except for the insecurities of malpractice, a good deal of this sort of effort really begins with education.

Mr. ROGERS. Yes. That is why I wonder if it is not well to have the radiologist give an official position, because the on-line physician is saying, Well, I have to have that X-ray to cover myself. The physician said, Look, you don't really need a skull X-ray because these criteria are not present.

Mr. CARTER. Mr. Chairman.

Mr. ROGERS. May I just finish this, and I certainly will yield. In that instance, it will be helpful for the physician to avoid any malpractice simply by saying, I was willing to have it; I called for it but the specialist there, the radiologist said it was not needed and, based on the criteria, it is not needed, and all of the scientific community agrees to that.

That is why I wonder if you really shouldn't be a consultant and official to give approval. That was my thinking.

What is your reaction, Doctor?

Dr. WENER. Who is going to cover the radiologist?

Mr. CARTER. Mr. Chairman.

Mr. ROGERS. Your scientific brethren.

Mr. CARTER. No, sir. The neurosurgeon was the one who was consulted about it first to determine if there should be an X-ray.

Mr. ROGERS. On every skull in the emergency room?

Mr. CARTER. According to Dr. Phillips in Washington, yes.

Mr. ROGERS. In the emergency room?

Mr. CARTER. Yes.

Mr. ROGERS. I doubt there is a neurosurgeon in every emergency room.

Mr. CARTER. Just as many as there are radiologists.

Dr. WENER. Let me make a comment about this, if I may.

Mr. CARTER. If you will read that, you will see these people were examined by a neurologist or a neurosurgeon.

Dr. WENER. This is for the purposes of that study. This is quite true. The critical point is that the presence or absence of a linear nondepressed skull fracture is of no clinical significance in virtually all cases. The only time that becomes a factor is when it causes internal bleeding or when the fragments of the fracture are, in fact, depressed. To demonstrate it is a radiographic exercise. It doesn't do anything as far as the care of the patient is concerned, yet I venture to say to you, if a patient were to walk into an emergency room having struck their head in an automobile accident and if the physician in the emergency room rightfully adjuged that he did not have to X-ray that patient and dismissed the patient with an ice pack and a couple aspirins and 2 or 3 days later with a persistent headache and now a swelling that is beginning to soften and get a little mushy, the patient walks into another physician's office and that physician does get an X-ray, I can almost promise you that a malpractice suit is going to be initiated.

Mr. ROGERS. But what does the x-ray show?

Dr. WENER. It shows a skull fracture, a linear, nondepressed, nonconsequential skull fracture.

Mr. ROGERS. So no damage?

Dr. WENER. No damage. Yet the courts will hold in today's climate that the first doctor who did not order that X-ray was negligent. If that first doctor is the physician who examined the patient in the emergency room, he is liable. If he says, I want a skull X-ray and the radiologist says you don't need one, and rightfully so, the radiologist is liable.

Mr. ROGERS. Let me ask this. What will the other radiologist testify?

Dr. WENER. The other radiologist will come in and testify to that. This is not a scientific treatise before your peers.

Mr. ROGERS. I understand. I understand the jury system and I understand it is a bother. But until some cases like that are established where you set forth the defense, this is always going to happen. If you have a proper defense, that is about the most you can hope for, because anybody can bring a suit against you.

Dr. WENER. That is true.

Mr. ROGERS. I don't think we can do all of the medicine on a definitive basis.

Dr. WENER. Unfortunately, Mr. Rogers, a lot of it is.

Mr. ROGERS. I understand that. That is what we have to get away from, if we can. If we have proper defenses and if there is the proper assumption of liability, then I think we will be able to get on top of the problem some. Then the general surgeon, or whoever made the initial judgment to refer him to the radiologist and the radiologist assumes his rightful consulting position and gives the intelligent judgment in the answer, you can't hold the first physician, and your peers would agree with you and the scientific evidence will support it.

Dr. WENER. But unfortunately, the jury system doesn't allow for that.

Mr. ROGERS. I think it does. There is no loss to him if there is no damage, and you can't get any money if there is no damage.

Dr. WENER. That, legally, is true, Mr. Rogers. You are 100 percent right.

Mr. ROGERS. I am sure there may be a few cases. But generally, I think you will find that if there is no damage, that can be brought out.

Dr. **Gehrig**. Let me take it from another point of view, because you put the radiologist in the position, on the basis of seven points of diagnosis, saying an X-ray is not required.

I think it is clear from what you said that you are not anticipating that the radiologist, per se, would have done that exam. A well-intentioned physician could have done the exam and missed an inequality pupil or some other aspect of a neurological examination that was important.

He didn't have that; he asked for a skull film, at any rate. The radiologist, in turning it down, turns it down on the basis of a believed adequate exam. I think he is defenseless at that point.

The other guy covered himself by having the film. This is in a situation where the fracture was a little depressed. If you allow the radiologist merely to say, if you haven't found these seven, you can't have the film, I think you leave him very, very liable.

Mr. **Caldwell**. May I comment a moment to your questions? What can we do about this? I don't know what you can do, and I don't know what the hospital association can do. I know if there are criteria related to whether skull X-rays ought to be taken or not, that I have a responsibility to see our emergency room staff is well familiar with those criteria and use them.

It seems to me that is the focus of this, maybe not the radiology department, because it is the emergency room staff that is doing these examinations and making these determinations.

Mr. **Rogers**. Are you aware of these standards?

Mr. **Caldwell**. I am not aware of them, no, sir.

Mr. **Rogers**. Is there any reason why AHA could not make hospitals aware of these standards?

Dr. **Gehrig**. I would have anticipated that this, however, might more typically have come out through the professional journal in the American College of Radiology or one of those. I know of no reason why they couldn't be.

Mr. **Rogers**. It seems to me you want to get all this knowledge out to hold down cost.

Mr. **Carter**. Mr. Chairman.

Mr. **Rogers**. Yes?

Mr. **Carter**. Actually a radiologist takes the films and interprets them. It is not his position to examine the patient to see if there is a possible fracture; he is not the one to do that. You are bringing the wrong man in here, to examine the patient.

Mr. **Rogers**. What is his role?

Mr. **Carter**. His role is just what I said. His role is to take the film, interpret it and determine whether there is a fracture whatever it is.

Mr. **Rogers**. He has no judgment as to the procedure getting the results that would be needed?

Mr. **Carter**. He does not examine the patient.

Mr. **Rogers**. I am not saying that.

Mr. **Carter**. You are saying he should make the evaluation as to whether the X-ray should be made or not. This involves the cranium, the brain, the cerebellum, the cerebrum and so on, and that is a problem. If you want this to be done by a specialist, it will have to be a neurosurgeon or neurologist.

Mr. **Rogers**. I doubt if everyone is seen by a neurologist.

Mr. **Carter**. I doubt everyone could be done by radiologists. There are not enough radiologists either to make that decision. We would be putting the wrong man in the wrong place.

Mr. **Rogers**. What is his job then?

Mr. **Carter**. Just what I told you; to take films and interpret them, and that is exactly what he does.

Mr. **Rogers**. That is not the judgment——

Mr. **Carter**. Perhaps we should consult the dictionary.

Mr. **Rogers**. Dr. Wener said——

Mr. **Carter**. All right, let's get our dictionary, and we will look it up and see what it says.

Mr. **Rogers**. What I am saying is, as I understand, they say they are trained and have a responsibility to determine if a procedure is proper; is that correct or not?

Doctor? I will get you in on this argument.

Dr. **Wener**. I was afraid you would.

Mr. **Carter**. I will even go back to that testimony given yesterday by the doctor from Washington. You will find in that testimony that the examination was done by a neurologist or neurosurgeon.

Mr. **Rogers**. I didn't say he had to examine. He has to determine whether the X-ray will bring back what is necessary to make the judgment.

Mr. **Carter**. How can he do that except by an examination?

Mr. **Rogers**. Because he knows the procedure and what comes forth from an X-ray that your general surgeon doesn't.

Mr. **Carter**. He can't tell by looking at a man what an X-ray is going to show; not at all.

Mr. **Rogers**. But he knows——

Mr. **Carter**. When he described that linear fracture, I believe what he had in mind was a tear in the middle meningeal artery.

Am I right on that, Doctor? Dr. Gehrig, will you speak up?

Dr. **Gehrig**. I believe that there is a common ground here, because you are suggesting, I think, Mr. Chairman, really that this man, without the benefit of doing an examination, flatly refuses to take a skull film that another physician in conscience has ordered. I think that is going too far.

Mr. **Rogers**. Wait a minute. Let me ask this: Suppose the guy comes in with a fractured shoulder and the doctor says, I want a skull X-ray. What would you do, Dr. Wener?

Dr. **Wener**. I will tell you what happens at the Greater Southeast. The technologist will walk in and say emergency has ordered a skull X-ray on this guy who is complaining of a pain in the shoulder. What I will do is get up and examine the patient.

At that point, I will determine if his shoulder is, in fact, hurting and call the emergency room and say, Dr. Smith, this guy has a shoulder pain; do you really want a skull?

He said, I saw 26 patients in the last 15 minutes. It should be a shoulder, and that is the way it is.

Mr. **Rogers**. That is what I thought your role would be.

Dr. **Wener**. Sure.

Mr. **Rogers**. I don't think we are in disagreement.

Mr. **Carter**. Well, I still think we are.

Mr. **Rogers**. I don't think so.

Mr. **Carter**. I won't retreat.

Mr. **Rogers**. I am not asking you to retreat. I don't think we are in disagreement.

Mr. **Carter**. Yes, sir.

Mr. **Rogers**. I think there is a proper role for radiologists to play.

Mr. **Carter**. You brought up something unusual: a man who has a fracture of a shoulder and who the doctor sends to get an X-ray of the skull.

Mr. **Rogers**. Both, defensive medicine.

Dr. **Wener**. If I may.

Mr. **Rogers**. Say he doesn't need the skull X-ray——

Dr. **Wener**. I think the point Dr. Carter makes in regard to the Bell and Loop study is critical to what we were speaking of, Mr. Rogers. If you have qualified specialists such as a neurologist——

Mr. **Carter**. You are a qualified specialist, are you not; a board certified radiologist?

Dr. **Wener**. Yes, sir. It just so happens I happen to be a neuroradiologist, so I will further complicate the matter. Be that as it may, when you have people like a neurologist and surgeons examining these patients and making these judgments, clearly this is superior to the usual examination administered in an emergency room setting.

I think if you could guarantee every skull injury, that kind of medical judgment that the role of the radiologist really would be reduced to simply interpreting the films. As it stands, that would be the setting in which you could say to the patient and the patient's lawyer, No, you don't need a skull X-ray. And you might have a skull fracture and it doesn't make any difference. So go home and put an ice pack on it and take two aspirin, and then be prepared when the suit comes up to have his peers say he did absolutely correct.

Unfortunately, as you may well know, and you made the point, that is not the type of medical expertise that is normally available to the routine emergency room visit. I think that is one of the areas in which we have a problem.

Mr. **Rogers**. If the various hospitals start using these procedures, that becomes the accepted practice. I won't pursue that anymore.

I notice in your accreditation you say all diagnostic radiologic equipment should be calibrated once a year unless no qualified personnel are available; then every 2 years. I am not sure I follow that.

Dr. **Gehrig**. You are referring to the Joint Commission on Accreditation Standards?

Mr. **Rogers**. Yes.

Dr. **Gehrig**. To the best of my knowledge, it recognizes real fact in some areas. I think you will find, and I think Dr. Wener might mention that in institutions like his, in most areas as a matter of fact, in talking with a number of institutions, if, for example, any machine is down for any reason at all, an automatic hold is placed on it until there is total reevaluation of the machine and its calibration.

Mr. **Rogers**. Is there any guidance on how quickly an out-of-compliance or out-of-adjustment machine must be repaired?

Dr. **Wener**. I don't really know.

Mr. ROGERS. Or whether it should be withdrawn from service?

Dr. WENER. It should be withdrawn from service until it comes into compliance. But how quickly you get it back up is a function of how badly you need the unit, I would think.

Mr. ROGERS. Does the hospital association have anything on that?

Dr. GEHRIG. No. Ours is only through the support of JCH and their accreditation methods.

Mr. ROGERS. Dr. Carter, do you have any more questions?

Mr. CARTER. Yes, I have another one.

Dr. Wener, suppose a patient is sent to you and films are requested from cardiac catheterization. And suppose you don't feel that that man has coronary sclerosis sufficient to justify this X-ray.

Do you make that judgment or do you go ahead?

Dr. WENER. We don't do the cardiac caths. The cardiology people do. So actually, that particular judgment would really never come before me. If the cardiologists involved, whom I presume are adequately trained people to satisfy our board's criteria for the granting of privileges to practice in the hospital, if they have adjudged that that patient needs a particular procedure, we of course would supply the technical support necessary to supply the necessary films. But I wouldn't get involved in making that judgment.

Mr. CARTER. They do take films of the coronary arteries, do they not?

Dr. WENER. Yes, sir.

Mr. CARTER. Don't you do this?

Dr. WENER. Yes, sir.

Mr. CARTER. Would you refuse to do it?

Dr. WENER. I am saying that cardiologists do that procedure. We supply the technical support for that.

Mr. CARTER. You take the films, in other words?

Dr. WENER. Yes, sir, the technologists do.

Mr. CARTER. That bears out what I said; the cardiologist makes a decision.

You are a very unusual man. You say in addition to being a radiologist, you are a neuroradiologist; is that correct?

Dr. WENER. Yes, sir.

Mr. CARTER. You have had special training then in diagnosis of head injuries and injuries to nerves where this might happen. Is this correct?

Dr. WENER. Yes, sir.

Mr. CARTER. So if a patient has a dilated pupil or something of this nature or any other weakness on the side opposite to where you described a rupture of a middle meningeal artery, you would be able to handle it. You are an unusually qualified man. In most cases still, my opinion keeps. In a head injury, there is nothing like a neurosurgeon or neurologist to make that decision. You are one that is qualified.

Dr. WENER. I quite agree with you; a neurologist or neurosurgeon should make that decision even in the case of——

Mr. ROGERS. Do you make any judgment on the encephalogram?

Dr. WENER. We really do.

Mr. ROGERS. Suppose a doctor wanted some encephalograms; could you refuse that?

Dr. WENER. Yes, sir, and I have.

I think we ought to correct something here. This is not an adversary proceeding. Usually it is a neurosurgeon or neurologist who has a patient, for instance, with eye symptoms, and identifies a large tumor of a portion of the bony skull. They will come down and say, look, we think we have this patient who has a problem with the pituitary gland.

In today's technology, what I will say is let's try it on the CAT scan. If we get the information we need from the CAT scan, then go do neurosurgery. If not, then I will do the pneumo.

But there were times when this would be an automatic requirement for a pneumo, and happily those times have passed because that is really sort of a lousy examination to have to inflict on anybody.

Mr. CARTER. If both tests are negative and he still has lateral hemianopsia and evidence of increased intercranial pressure, what are you going to do?

Dr. WENER. I think the clinical setting you are describing is going to leave that man to be operated on because he needs the surgery. It is not a question of whether to operate or not. If there is no super sellar extension of the tumor, as identified from the——

Mr. CARTER. Surgery, right?

Dr. WENER. Yes, sir.

Mr. CARTER. Thank you.

Mr. ROGERS. Thank you. Your testimony has been most helpful, and if the AHA could get some of that information out, it would be good.

Dr. GEHRIG. Yes, sir, we will do all we can.

Mr. ROGERS. Thank you.

The committee stands adjourned until 10 o'clock tomorrow.

[Whereupon, at 4:45 p.m., the subcommittee adjourned, to reconvene at 10 a.m. Friday, July 14, 1978.]

EFFECT OF RADIATION ON HUMAN HEALTH

Radiation Health Effects of Medical and Diagnostic X-Rays

FRIDAY, JULY 14, 1978

House of Representatives,
Subcommittee on Health and the Environment,
Committee on Interstate and Foreign Commerce,
Washington, D.C.

The subcommittee met, pursuant to notice, at 10 a.m. in room 2123, Rayburn House Office Building, Hon. Paul G. Rogers, chairman, presiding.

Mr. Rogers. The subcommittee will come to order.

Today we will continue oversight hearings on radiation health effects of medical and dental diagnostic X-rays.

Our first witness this morning Dr. Arthur C. Upton, Director of the National Cancer Institute, together with members of his staff.

Your statement will be made a part of the record.

STATEMENT OF ARTHUR C. UPTON, M.D., DIRECTOR, NATIONAL CANCER INSTITUTE, NATIONAL INSTITUTES OF HEALTH, PUBLIC HEALTH SERVICE, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE, ACCOMPANIED BY JOHN D. BOICE, JR., PH. D., ENVIRONMENTAL EPIDEMIOLOGY BRANCH, DIVISION OF CANCER CAUSE AND PREVENTION; RICHARD D. COSTLOW, PH. D., DIVISION OF CANCER CONTROL AND REHABILITATION; AND WILLIAM POMERANCE, M.D., DIVISION OF CANCER BIOLOGY AND DIAGNOSIS

Dr. Upton. Thank you, Mr. Chairman and members of the subcommittee. I am pleased and honored to appear before you today to discuss the subject of diagnostic radiation, the possible hazards of diagnostic radiation exposure, and the National Cancer Institute's involvement in this area. Appearing with me to answer questions are members of my staff: Dr. Richard Costlow of the Division of Cancer Control and Rehabilitation; Dr. Fink was unable to come today; Dr. John Boice of the Environmental Epidemiology Branch, Division of Cancer Cause and Prevention; and Dr. William Pomerance of the Division of Cancer Biology and Diagnosis.

Mr. Rogers. We welcome all of you to the committee.

Dr. Upton. Thank you, sir.

The question of risks associated with diagnostic radiation is complex. Except for a few fluoroscopic procedures, diagnostic X-irradiation involves doses of radiation that are relatively low, of the order of millirads or only a few rads, as compared with those characteristic of therapeutic radiation which involve hundreds or thousands of rads. Studies drawn from a variety of sources—therapeutic radiation, A-bomb survivors, and multiple fluoroscopic procedures—substantiate the risk of cancer following irradiation at levels in excess of 50 rads; however, the risk of cancer following irradiation at diagnostic dose levels remains uncertain.

There are few empirical indicators of risk in this dose region, one notable example being an association between prenatal exposure and an increased risk of developing cancer subsequently in childhood. I believe, however, that the risks are generally so low in diagnostic radiation it is nearly impossible to derive useful estimates of them from study populations of manageable size. Estimates are, therefore, produced primarily by extrapolation, based on theoretical knowledge of dose-effect relationships which involves unproven assumptions and large uncertainties.

It is widely accepted that although risks of low-level radiation may be very small, there is probably no level of exposure entirely without some risk. Yet unknown is whether the dose-response relationships which have been established through studies at higher levels of exposure have any bearing on the degree of risk at low levels of exposure. Many radiobiologists take the position that we simply have no way of estimating reliably the carcinogenic risks attached to doses below a few rads.

Some argue that the use of dose-response relationships derived from high dose data will lead to overestimation of risks in the low-dose region. Others argue just the opposite. Nevertheless, low-dose estimates must be made, and until there is hard evidence, they can be made only by extrapolation from the higher-dose regions where adequate observations exist.

Compounding the difficulty in assessing the degree of risk is the range of exposure involved. The 1977 report of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) states that:

> The organ doses received in diagnostic radiology may range over four orders of magnitude (from a few millirads to a few tens of rads) and will usually be given at high dose rates, compared with other manmade and natural sources.

The various effects of radiation, the report goes on to say—

> * * * depend in a complex manner on the dose, the part of the body exposed, the dose rate and the length of time during which the total dose was received * * *. Therefore, the detailed estimation of the risk from medical exposure is very complex * * *.

For example, a cardiac catheterization procedure involves a median exposure level per examination of 20-30 roentgens. Computerized tomography scanning involves doses ranging from 2 to 6 rads. At the low end of the spectrum, a typical chest X-ray exposes the individual to about 20 milliroentgens.

Not only is there a broad range of exposure, depending on the organ to be irradiated, there is also a range of radiosensitivity from one organ and tissue to another. The published studies suggest the fetus, bone marrow, female breast and thyroid are among the more radiosensitive tissues as concerns radiation carcinogenesis.

Studies of the repeated use of fluoroscopic examinations of the chest in monitoring the pneumothorax treatment of tuberculosis are noteworthy in relation to risk estimates for breast cancer.

Although the total doses received by patients thus treated averaged more than 100 rads in one series of patients, the dose to the breast at each fluoroscopic examination was only approximately 1.5 rads. Nevertheless, the carcinogenic effect on the breast tissue of the cumulative exposure in such patients appears to be the same as that seen in other patients following single large total doses of equivalent size.

Other studies have shown that breast tissue seems to be particularly sensitive to ionizing radiation during periods of rapid growth, such as during menarche and during the first pregnancy. Thus, it is difficult to make broad estimates of the degree of risk associated with low-level radiation exposure without knowing the tissue type involved and whether the tissue was undergoing rapid cell division at the time of exposure.

Based on my knowledge of this field, I would consider the risk estimates presented in 1972 by the National Academy of Sciences Advisory Committee on the Biological Effects of Ionizing Radiation [see attached table p. 699] to remain valid today for purposes of radiological protection. These estimates were based on a linear, nonthreshold, dose-incidence extrapolation model and are consistent with the estimates published more recently by the United Nations Scientific Committee on the Effects of Atomic Radiation (1977), also reporting last year, and the International Commission on Radiological Protection (1977) also reporting last year.

Compounding the question of the risk of diagnostic radiation is the counterbalancing question of benefit. The advances in medical practice made possible by diagnostic X-rays do not need to be enumerated here today. In discussing most types of environmental exposure, risk and benefit are weighed in terms of society as a whole. In the case of diagnostic radiation, risk and benefit are usually limited to the individuals irradiated. The issue of benefit versus risk must be decided on a case-by-case basis. Such questions as: What do we hope to learn through this procedure? How will X-ray findings enhance appropriate management of this case? Is there an alternative other than X-ray to gaining this information? must be considered in weighing benefit versus risk.

It is generally accepted that no diagnostic X-ray procedure should be undertaken unless it is indicated medically, and then, every precaution should be taken to keep the dose level as low as is achievable, consistent with good image quality. Routine monitoring and calibration of the apparatus are the best ways to assure that the lowest exposure levels possible are being maintained. Care should be taken that only that area to be visualized is exposed and that surrounding tissue is shielded. The question of benefit versus risk should be weighed, and the expected benefit judged to outweigh the presumed risk.

I believe these issues and recommendations for diagnostic X-ray use are addressed in the guidelines recommended jointly by the Assistant Secretary for Health and the Administrator of the Environmental Protection Agency, approved by the President on January 26 of this year, and published in the Federal Register February 1, 1978. Such precautions seem to be in the best interest of everyone involved.

I would like to turn now to the research activities of the National Cancer Institute involving medical uses of radiation. I reviewed many of these with you during my visit with this subcommittee in February. Therefore, I will now list them only briefly. These activities include studies of women who underwent radiation treatment for postpartum mastitis; studies of children who were administered low-dose iodine-131 during diagnostic tests of the thyroid; a study of children who were irradiated for enlarged tonsils; and an international study of women who have undergone radiation treatment for cervical cancer, as examples.

In addition to epidemiologic evaluations of the risk of diagnostic radiation exposure, we are funding basic studies of radiation carcinogenesis in experimental animals and cell systems to determine the mechanisms by which radiation exposure induces carcinogenic cell changes and the ways in which these changes might interact synergistically with other factors such as hormones, rate of cell growth, or smoking.

It is true that during the 1950's the National Cancer Institute had a relatively more active radiation carcinogenesis program than has existed in our recent past. In order to refocus some of the emphasis on radiation that became diffused within the Institute at the end of the 1950's, we now plan to establish a working group within the NCI to review and coordinate Institute programs and to assess the needs for continued and new areas of research. I am certain that diagnostic radiation will be on our agenda.

The National Cancer Institute is involved in a number of clincal programs that make use of medical radiation. These include a limited screening program of persons at high risk for lung cancer, to determine whether screening of predetermined groups will lead to earlier detection and improved treatment; a colon cancer screening program involving fluoroscopic procedures at doses of 3 roentgens, as opposed to a general level of from 2 to 12 roentgens; a study of optimal uses of computerized tomography to both the head and the body; and, finally the breast cancer detection demonstration projects.

The breast cancer screening projects, were established to demonstrate methods of screening women 35 to 74 years of age for breast cancer. The basis for their establishment was the finding of the health insurance plan of Greater New York study, that screening had reduced breast cancer mortality in women over 50 years of age. It was believed that since breast cancer is the majority killer of women between the ages of 40 and 44, and that since a cancer begins developing long before it is palpable, it would be beneficial to begin screening women before they reached the age of 40.

However, serious questions about the safety of routine mammography were raised publicly by Dr. John Bailar of the National Cancer Institute in 1975. Three ad hoc committees were appointed by the Director of the Institute to respond to these questions. They were asked to estimate the gross and net benefits of adding mammography to history and physical examination in the Health Insurance Plan Study of the 1960's; to review the histology of breast cancer cases detected through this study; and to evaluate the relationship between benefit and risk in mammographic screening. I was privileged to chair one of these committees.

On July 19, 1976, the committees made preliminary reports. These led to issuance of guidelines for operation of the screening projects, which suggested that since no proof of benefit in mammographic screening had yet been shown for women under the age of 50, and since there was presumption of some radiation-induced risk, an asymptomatic woman under 50 should not be screened with mammography unless she were at high risk, and I quote, "due to family history, reproductive history, prior breast cancer or tumor, et cetra."

In those instances, the guidelines went on, the risks and benefits should be fully explained and the final decision made between her and her physician. At that time, it was agreed that mammography should not be "withheld from a woman 35 to 50 years old if she and the physician agree that it is in her best immediate interest."

It was further advised that radiation dosage must be "kept to the lowest dose consistent with good image quality." Although the maximum dose was not specified in the guidelines, project directors were notified that exposure levels should not exceed one rad per breast per examination.

It was noted that participants should be informed that mammographic equipment was routinely monitored and that monitoring procedures were checked by experts in radiation physics. Because of concern over low-level radiation risks, mammography equipment has been improved and improved again. Mammographic screening now can be offered at dose levels of one-tenth to two-tenths of 1 rad or 100 to 200 millirads, which represent a significant reduction from an average dose of roughly 2 rads less than 3 years ago.

In March 1977, the committee submitted their final reports to the Director of the Institute. Following review of the reports, the guidelines were modified to limit mammographic screening of women between the ages of 35 and 49 to those with a personal history of previous breast cancer or whose mothers or sisters had had breast cancer. This limitation became a project requirement rather than a recommendation. A working group was convened in January 1977, to review the findings to date from the screening projects to determine whether there were sufficient data to draw conclusions about the benefits of mammography to younger women.

In September 1977, the working group presented its report during a 3-day National Institutes of Health consensus meeting on breast cancer screening. The working group recommended that the use of mammography be further limited for women in the 35 to 40 age group to only those with a prior history of breast cancer. The group concurred with other limits previously outlined in the guidelines. The consensus panel concurred with this recommendation and further suggested that each woman be advised to maintain a personal record of all radiation she receives, using dosage level information to be included in the informed consent form.

This is where the projects stand today. Screening is continuing to the end of the 5-year demonstration program, with physical examination and mammography for women age 50 and over and for younger women in high-risk groups, and with physical examination alone for those younger women who do not fall into the high-risk categories.

I mentioned that the mammographic equipment used in the screening projects is monitored regularly and calibrated annually. This function is carried out by six regional Centers for Radiological Physics, operated under contract with the Institute's Division of Cancer Control and Rehabilitation. In brief, the purpose of these Centers is to insure high quality radiological physics at radiotherapy facilities associated with our programs; to serve as a consultative and educational resource for physicists, physicians, and allied health personnel in each of their respective regions; and to monitor exposures to screenees at the breast cancer detection demonstration projects.

In addition to developing the instruments now used to check mammographic equipment in the field, the Centers for Radiologic Physics have been responsible for a mail-in monitoring system. Through the use of small measuring devices known as thermoluminescent dosimeters (TLD's), each screening center routinely monitors the skin exposure to screenees. These dosimeters are mailed to the Centers for Radiological Physics for interpretation. Any problems with equipment are detected and corrected between routine calibration visits by Center staff.

To extend the technology developed for the screening projects, NCI is working with the Bureau of Radiological Health on a program known as BENT—breast exposure: nationwide trends. The objective of this program is to extend capabilities for mammographic monitoring to State health departments through a voluntary compliance program.

The purpose of monitoring systems is, of course, to make sure that proper exposure levels are being maintained. The National Cancer Institute is also working to reduce radiation exposure through development of lower-dose technology. We have earmarked $650,000 in FY 1978 research funds to develop methods for reducing dosage in computerized tomography scanning equipment and in mammography, with a goal of no more than 150 millirads or 0.15 roentgens surface exposure for mammography.

At the same time we are working to develop diagnostic techniques which do not require X-rays. Such alternatives, now undergoing testing, include ultrasound and thermographic technology and the use of immunologic, hormonal, or biochemical markers in the bloodstream or urine to detect cancer. In all, we have devoted close to $11 million to research in these areas.

Mr. Chairman, it is true that the latest research findings imply that even at the lowest levels of exposure there may be some risk from ionizing radiation. We are working to improve our knowledge of risks and to continue to reduce exposure levels through prudent use of diagnostic radiation; through development of systems for accurate monitoring of equipment; through development of safer, lower dose equipment; and through a search for diagnostic tools which may eventually eliminate the need to use radiation in the detection of cancer.

This concludes my testimony. I and my colleagues will be happy to answer any questions.

Mr. ROGERS. Thank you very much.

[Attachment to Dr. Upton's prepared statement follows:]

ESTIMATED RISKS OF RADIATION-INDUCED CANCER[a]

Age at time of irradiation	Type of cancer	No. of radiation-induced deaths per 10^6/yr/rem[b]	No. of naturally occurring deaths per 10^6/yr
Prenatal (in utero)	Leukemia	25	50
	All other cancer	25	50
0-9 years	Leukemia	2.0	40-50
	All other cancer	1.0	50-1300
10+ years	Leukemia	1.0	50
	All other cancer	5.0[c]	1500

[a] From report of BEIR Committee (1972); values in table have been rounded.

[b] Dose to whole body.

[c] The risk for those aged 10 or more at the time of irradiation for all types of cancer excluding leukemia can be broken down by respective sites as follows:

Types of Cancer	Deaths per 10^6/yr/rem
Breast (average for both sexes)	1.5
Lung	1.3
GI incl. stomach	1.0
Bone	0.2
All other cancer	1.0
Total	5.0

On this research that you have been doing in ultrasound and thermographic equipment, what result has come about to date?

Dr. UPTON. I might ask Dr. Pomerance to speak about the ultrasound studies since these fall in his area of expertise: ultrasound and thermographic technology.

Dr. POMERANCE. We have been involved with trying to develop specific mammographic equipment in ultrasound since 1972. We have developed equipment that is in the process of being finalized for clinical evaluation. We have expanded our interests in these particular areas so that we are looking not only at sonography but at other modalities of echosonography in order for us to facilitate this process and possibly demonstrate the existence of smaller masses. Such equipment is being built for us, again, in another institution. We are now doing new investigations looking at two new pieces of equipment that will be investigated for its possibilities and its contribution in the field of mammographic ultrasonography specifically.

Mr. ROGERS. From your work done to date, I understand you are in the process of undergoing clinical trials with the machine?

Dr. POMERANCE. We will have clinical trials probably within about a year. We have no ongoing clinical trials at this particular moment. I should say this involves at least four different pieces of ultrasound equipment that have been built for the National Cancer Institute specifically for recognition of breast masses.

Mr. ROGERS. What is the indication as to their adequacy in being substituted for radiation?

Dr. POMERANCE. Theoretically, they should be able to reproduce the results that we have had with X-ray mammography and perhaps even do a little bit better. This will have to be demonstrated, of course, clinically.

Mr. ROGERS. Is there any delay in help or the funding of people involved which could be overcome in order to accelerate clinical trial?

Dr. POMERANCE. No; I do not believe there is any delay at this time.

Mr. ROGERS. It is moving as rapidly as possible?

Dr. POMERANCE. In fiscal year 1978 our involvement is about $1.25 million.

Mr. ROGERS. Who is building the machine for you?

Dr. POMERANCE. There is a machine that has been built for us and being modified at the present time at the Albert Einstein Medical Center in New York. There is a machine that is being built at the Mayo Clinic, and there are two recently introduced machines, one of which is an Australian machine and has been brought to this country, and one is a machine that was developed by RCA and is now being merchandised by Johnson & Johnson.

The last two machines are at the Jefferson Medical Center in Philadelphia, and both will become available within about a year for good clinical trials.

Mr. ROGERS. Theoretically, could this technique, the ultrasound, replace the technique of the X-ray and the CAT scanner?

Dr. POMERANCE. Theoretically, so far as the breast is concerned—the CAT scan is not yet applicable to the breast—but insofar as the applicability of the ultrasound, it can totally replace mammography if it can demonstrate the same degree of accuracy.

Mr. ROGERS. What I was thinking was for the scanner; can a machine be developed there to bring about the same results that you get from a scanner, not on the breast but elsewhere?

Dr. POMERANCE. Such a machine is being built for us at the Mayo Clinic at the present time.

Mr. ROGERS. That can be a substitute in effect for the scanner?

Dr. POMERANCE. That would incorporate some of the principles which I think the chairman is referring to.

Mr. ROGERS. So that there again we would reduce the use of radiation. What is the effect of the ultrasound? Do we know?

Dr. POMERANCE. It is being continuously looked into, and I do not think we would be in a position to state there is no risk.

Mr. CARTER. In the administration of ultrasound, we know it is used many times over arthritic joints and in cases of bursitis, where there is calcification in the deltoid region. But do you use ultrasound over the base of the neck?

Dr. POMERANCE. In therapeutic ultrasound, and the dosage is far, far higher than the dosage that is used in diagnostic ultrasound.

Mr. CARTER. Do you use it over the base of the skull, and the lower cervical vertebra?

Dr. POMERANCE. It is not used at the present time.

Mr. CARTER. Is it advisable to use it that way? Do the companies that make the ultrasound apparatus recommend this be done?

Dr. POMERANCE. Not that I am aware of, sir.

Mr. CARTER. Do you mean it can be used at the base of the brain?

Dr. POMERANCE. There is no interdiction against its use.

Mr. CARTER. It is my understanding that there has been.

Thank you, Mr. Chairman.

Mr. ROGERS. There has been concern about its use.

Mr. CARTER. Yes, that is right.

Mr. ROGERS. Is this for treatment or for diagnosis?

Mr. CARTER. This is for treatment.

Mr. ROGERS. What about for diagnostic use?

Mr. CARTER. I guess it would be a much lower range.

Mr. ROGERS. Anyhow, the possibility, and the institute is pursuing vigorously the possibility that technology will develop which will lessen the need for the use of radiation?

Dr. UPTON. That is correct.

Mr. ROGERS. Would you let us have a rather detailed explanation of this in the record of the various projects?

Dr. UPTON. I would be happy to provide a full breakdown.

Mr. ROGERS. And what you anticipate from this.

Dr. UPTON. Yes.

[Testimony resumes on p. 900.]

[The following information was received for the record:]

CONTRACT RESEARCH SUMMARY

Title: Lung Cancer -- Early Detection, Localization, and Therapy

Principal Investigator: Dr. John K. Frost
Name/Address Johns Hopkins University
Performing Organization: Baltimore, MD

Contract Number: NO1-CB-92172
Starting Date: 6/28/69 Expiration Date: 6/27/77

Goal: (1) Develop improved cytologic methods for sputum examination for the early detection of lung cancer; and (2) develop improved methods for the diagnostic localization of lung cancer (Phase I of Hopkins study).

Approach: The project follows groups of subjects who are at high risk of lung cancer: chemical and asbestos workers who are also cigarette smokers. They are tested by sputum cytology and x-ray studies. These studies are directed to the biologic significance of the morphology of mild, moderate and severe cell atypia by correlation with patient follow-up. Patients cytologically suspicious or positive for cancer are studied for better localization techniques, mainly with tantalum dust bronchography and fiberoptic bronchoscopy. Improved equipment is also under development. (See also NO1-CN-45037).

Progress: Clinical material was obtained from 2,165 cigarette smokers who are either asbestos or bis-CMME workers. Improved transbronchial television microscope was developed as well as new methods to diagnose cancer cytologically and histologically from areas of lung heretofore unaccessible. For x-ray negative lesion localization, controllable catheter tantalum bronchography and various instruments were developed for rigid and flexible fiberoptic bronchoscopy. Surgical techniques were developed for improved therapy of early lesions. Techniques evolved from this Phase I are used in Early Lung Cancer Cooperative Study. The project includes continuing investigation of biologic significance of cytologic high-suspect lesions; parameters for automatic recognition of lung cancer; development of transbronchoscope probes for mucosal tension, bronchial wall firmness, infrared sensing, thermorecovery, laser, electrocautery, and ultrasonic forceps; and development of clinical inhalation for tantalum bronchography.

Significance for Cancer Research (NCP Objective 5 Approach 4)
Early detection is the best present hope for improving the mortality from lung cancer.

Project Officer: Louis P. Greenberg
Program: Diagnosis
Technical Review Group: Diagnostic Research Advisory Group
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: Lung Cancer -- Early Detection, Localization and Therapy

Principal Investigator: Name/Address Performing Organization:	Dr. Myron R. Melamed Memorial Hospital for Cancer and Allied Diseases New York, NY

Contract Number: NO1-CN-45007
Starting Date: 9/1/73 Expiration Date: 8/31/78

Goal: To evaluate sputum cytopathology as a supplement to annual chest x-rays in detecting pulmonary neoplasms at an "early stage" and to evaluate the efficacy of techniques for prompt localization of radiologically occult lung cancer (e.g., before progression to x-ray positive); in general, to evaluate the efficacy of such screening to reduce lung cancer mortality.

Approach: Over a 3-year period, 5,000 test subjects and 5,000 control subjects will be entered into this study with active screening for 5 years, all to be followed for at least an additional 5-year period, for sufficient years to be statistically significant to answer pertinent questions. This will be conducted according to a protocol developed in conjunction with the Johns Hopkins University and the Mayo Foundation.

Progress: The early lung cancer detection program in New York is now in its fourth year. The study is being conducted by Memorial Sloan-Kettering Cancer Center using facilities at the Strang Preventive Medicine Institute for interviews and examinations of the subjects involved. To date, over 9,300 men have been examined; it is anticipated that 10,000-12,000 will be entered into the program to be followed for at least five years. All are cigarette smokers over the age of 45 years. A comparison will be made between randomly selected subjects having annual chest x-rays only, and subjects having 4-monthly sputum cytology as well as annual chest x-rays. In a preliminary evaluation of the first 6,612 men, the initial examination revealed 15 lung cancers, Stages II and III, and eleven lung cancers, Stages 0 and I. Of 3,387 men who had x-rays alone, there were 3 early cancers detected (Stage I); of 3,225 men who had x-rays and cytology, there were 4 early cancers detected by x-rays (Stage I) and 4 detected by cytology (Stage 0). In addition, 3 larynx cancers were detected by cytology.

Significance for Cancer Research (NCP Objective 5 Approach 4)

Project Officer: Louis P. Greenberg
Program: Lung Cancer Diagnosis
Technical Review Group: Diagnostic Research Advisory Group
Relevance Review Group: Institute Director and Executive Committee
FY 77 Funds: $875,246

CONTRACT RESEARCH SUMMARY

Title: Lung Cancer Control: Detection and Treatment

Principal Investigator:	Dr. John K. Frost
Name/Address	Johns Hopkins University
Performing Organization:	Baltimore, MD

Contract Number: NO1-CN-45037
Starting Date: 9/1/73 Expiration Date: 7/15/78

Goal: To determine the effect of the early detection of lung cancer by sputum cytology, followed by surgical removal of the tumor on long-term survival in the disease (Phase II of Hopkins Study).

Approach: The study population consists of males, 45 years or older, who smoke a pack or more of cigarettes a day. By random assignment from individuals responding to advertisement, it was planned to accumulate over several years two groups of over 5,000 each. The test group would receive sputum cytologic examination and chest x-ray every four months; the control group will have an annual chest x-ray. Subjects suspicious or positive for cancer would be carefully worked up, to include fiberoptic bronchoscopy; cancers would be removed surgically. All subjects will be followed for at least 5 years to determine actuarial survival. (See also NO1-CB-92172.)

Progress: Approximately 10,000 people have been screened to date in this project. A return rate of 3% was obtained from miscellaneous groups contacted by mailings; a return rate of 5% was obtained from the other subjects in industry and government. Screening was done at Johns Hopkins Hospital and Social Security office. Cancers are found to date in approximately 6 per 1,000 screenees (5.4/1,000 in the control X-group and 6.8/1,000 in the cytology C-group). For every 5 cases of lung cancer detected by chest x-ray there exist 2.06 additional cases of lung cancer detected only by cytology. Localization of these early lesions has been made by techniques of bronchoscopy and cytopathology. This project is carried on in conjunction with Mayo Clinic, Memorial Hospital, and University of Cincinnati in the NCI Cooperative Early Lung Cancer Group.

Significance for Cancer Research (NCP Objective 5 Approach 4)
Early cytologic detection, the best present hope for improving lung cancer mortality, requires rigid proof of its effectiveness.

Project Officer: Louis P. Greenberg
Program: Diagnosis
Technical Review Group: Diagnostic Research Advisory Group
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $1,095,000

CONTRACT RESEARCH SUMMARY

Title: Lung Project for Detection and Localization of Early Lung Cancer

Principal Investigator:	Dr. Robert S. Fontana
Name/Address	Mayo Foundation
Performing Organization:	Rochester, MN

Contract Number: NO1-CB-53886
Starting Date: 9/27/74 Expiration Date: 9/26/78

Goal: To improve methods of diagnosis of early lung cancer and to assess survival of patients with lung cancer detected by these methods.

Approach: A study population of 9,313 subjects was obtained from interviews of 11,000 non-volunteers. Subjects were Mayo Clinic outpatients who were men, 45 years old or more, smoking one pack of cigarettes or more daily. None had a history or suspicion of respiratory cancer on entry into the Clinic; all had a life expectancy of at least 5 years, and all were judged capable of tolerating pulmonary resection. The 9,313 study subjects were first screened by means of chest x-rays, 3-day sputum cytology tests and lung health questionnaires. This screening yielded 86 unsuspected ("prevalence") lung cancers, 16 detected by cytology alone, 53 by x-ray alone and 17 by both tests. Radiographically "occult" cancers were localized fiberbronchoscopically. Subjects with a "negative" initial screen were randomized into a close surveillance group, rescreened every 4 months, and a standard surveillance group ("control") advised to undergo rescreening once a year. Potential lung cancer "risk-factors," including aryl hydrocarbon hydroxylase (AHH) are also being evaluated, as are hemato-porphyrin derivative (HpD) and cryotherapy as techniques for "mapping" and treating carcinoma-in-situ.

Progress: As of April 1, 1977, both the close surveillance group and the "control" group have been observed more than 10,000 man-years, and 94 new ("incidence") cases of cancer of the respiratory tract had been detected, 17 involving the upper airway and 77 the lungs. In the close surveillance group there were 53 new lung cancers (only 13 of which were detected cytologically) and 15 lung cancer deaths. Early survival data in this group are encouraging, but much longer observation is needed. In the control group there were 24 new lung cancers and 14 lung cancer deaths, with a tendency toward more traditional lung cancer survivorship.

Significance for Cancer Research (NCP Objective 5 Approach 4)

Project Officer: Louis P. Greenberg
Program: Lung Cancer Diagnosis
Technical Review Group: Diagnostic Research Advisory Group
Relevance Review Group: Institute Director and Executive Committee
FY 77 Funds: $998,000

CONTRACT RESEARCH SUMMARY

Title: Statistical Center for Cooperative Lung Cancer Groups

Principal Investigator: Name/Address Performing Organization:	Dr. C. Ralph Buncher University of Cincinnati Medical Center Cincinnati, OH

Contract Number: N01-CB-43868
Starting Date: 6/1/74 Expiration Date: 5/31/79

Goal: To collect and analyze data from the three collaborating lung cancer groups in the lung cancer screening program directed toward the detection of early lung cancer in high risk patients to see if this screening will reduce mortality and morbidity.

Approach: Procedures have been established and agreement has been reached concerning the common data base for this study. The data are being monitored by the Statistical Center, entered into the computer and analyzed. Reports are being made quarterly. The Statistical Center will search the data for significant statistical findings.

Progress: In the Cooperative Early Lung Cancer Group program, the Cincinnati Central Statistical Group (CSG) has established a common data base, made suggestions for uniform data recording by the clinical centers, and reported results to the NCI and participating clinical centers. The CSG receives patient data from each of the clinical centers and forms a master patient file from which tables, reports, and analyses can be derived to answer the questions of the study, i.e., whether efforts directed toward earlier diagnosis have successfully led to improvement in mortality from lung cancer.

Tables showing the results and status at each of the clinics are produced. They have proven of value to the NCI and other participants as a means of monitoring the progress and results of the study. Patients' status indicator codes and information on follow-up have been added to the common data base, and computer programs for editing submitted information have been developed. In the past year, programs to calculate person-years of risk were developed and mortality records have been computerized.

This contract includes similar work in a three-center study of pancreatic cancer and a five-center study of brain cancer.

Significance for Cancer Research (NCP Objective 5 Approach 4)

Project Officer: Louis P. Greenberg
Program: Diagnosis
Technical Review Group: Diagnostic Research Advisory Group
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $220,089

CONTRACT RESEARCH SUMMARY

Title: Detection of Pancreatic Cancer at Early or Small Stage Prior to Metastasis

Principal Investigator:	Dr. Patrick J. Fitzgerald
Name/Address	Memorial Hospital for Cancer and
Performing Organization:	Allied Diseases
	New York, NY

Contract Number: NO1-CB-43975
Starting Date: 6/1/74 Expiration Date: 8/31/77

Goal: To evaluate diagnostic methods and findings in patients undergoing abdominal exploration for supposed pancreatic cancer in order to establish a base that can be used for the detection of small pancreatic cancer before metastasis that may lead to an increase in the 5-year survival from 1% now prevalent to 13% or more.

Approach: Three cooperating institutions will study, in a predetermined manner by a common protocol, patients who are suspected of having cancer of the pancreas and are about to undergo abdominal surgery. Special studies delineated in the protocol will include preoperative and operative study of CEA in peripheral and portal venous blood. Special studies of pancreatic excretions obtained through a fiberoptic scope in the duodenum, pancreatic and biliary ducts will be undertaken. Such secretions will be studied for tumor-associated antigens, abnormal enzyme content, biochemical alterations, as well as cytological changes which will permit the earlier diagnosis of pancreatic cancer.

Progress: In 31 months about 1,050 patients with abdominal complaints were seen by the Pancreas Study Group. Of these patients, 160 (15%) were suspected of having pancreatic cancer and 76 (64%) were found at operation to have it. Twenty-two patients (43%) had "curative" resections; 13 of these are living 2-20 months postoperatively. The operative mortality (death within 1 month) was 18%. In 43 other patients, at operation, 32 had non-pancreas cancer and 11 had noncancerous diseases. Computerized transaxial tomography was the most accurate diagnostic technique -- it diagnosed all 28 cases of proven pancreas cancer on whom it was tried but it gave 4 false positive diagnoses (2 cases of pancreatitis). Celiac arteriography diagnosed about 80% of cases with about a 20% false positive rate. Ultrasonography and selenium-75 scanning were less helpful. Carcinoma *in situ* was found in a small percentage of cases. Of about 15,000 asymptomatic patients screened at the Strang Clinic Institute, 15 were proven to have gastrointestinal cancer, but no case of cancer of the pancreas was found (about 2 cases were expected from incidence rates). Subsequently, 2 of the 15,000 patients were said to have died of pancreas cancer.

Significance for Cancer Research (NCP Objective 5 Approach 3)

Project Officer: Louis P. Greenberg
Program: Diagnosis Site Visit Date: 3/21/77
Technical Review Group: Diagnostic Research Advisory Group
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: Detection of Pancreatic Cancer at Early or Small Stage Prior to Metastasis

Principal Investigator:	Dr. A. R. Moossa
Name/Address	University of Chicago
Performing Organization:	Chicago, IL

Contract Number: N01-CB-43976
Starting Date: 6/30/74 Expiration Date: 6/29/77

Goal: To evaluate diagnostic methods and findings in patients undergoing abdominal exploration for pancreatic cancer to establish a base that can be used to detect small pancreatic cancer before metastasis that may lead to an increase in the 5-year survival from 1% now prevalent to 13% or more.

Approach: Using a common protocol, three institutions will study patients suspected of having pancreatic cancer and about to undergo abdominal surgery. Studies will include preoperative and operative study of CEA in peripheral and portal venous blood. Pancreatic secretions will be studied for tumor-associated antigens, abnormal enzyme content, biochemical and cytological changes.

Progress: To date, 148 patients have been referred to this study. Of these, five patients had positive diagnosis of pancreatic cancer elsewhere and came to the hospital for radiotherapy and/or chemotherapy treatments. Systemic blood was taken, but no additional investigation was performed. Of the 143 patients entered into the study, 73 have been fully, and 70 partially, investigated. Of the 73 who completed the protocol, 50 have undergone laparotomy, and 24 pancreatic cancers were found. Of the 23 patients who completed the protocol and did not undergo laparotomy, none has developed pancreatic cancer, and all have been followed up from 6 months to 2 1/2 years. Of the 70 who were partially investigated, 46 underwent laparotomy, and 17 pancreatic cancers were found. The remaining 24 patients who were partially investigated did not undergo laparotomy, and two of them had pancreatic cancer diagnosed by biopsy and confirmed by autopsy.

On the basis of this study, the rational sequence of testing appears to be duodenal drainage studies, abdominal ultrasound, and liver scanning in the first instance. Patients with any documented abnormality and without evidence of metastases should undergo ERCP and arteriography. A pancreatic oncofetal antigen was partially purified and characterized and a quantitative rocket immunoelectrophoresis was developed to study its distribution in patients with various disorders. A high incidence of carbohydrate intolerance in patients with pancreatic cancer was demonstrated and a substantial decrease in insulin release following a standard glucose load in these patients was established.

Significance for Cancer Research (NCP Objective 5 Approach 3)

Project Officer: Louis P. Greenberg
Program: Diagnosis Site Visit Date: 3/22/77
Technical Review Group: Diagnostic Research Advisory Group
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: Detection of Pancreatic Cancer at Early or Small Stage Prior to Metastasis

Principal Investigator: Dr. Vay Liang W. Go
Name/Address Mayo Foundation
Performing Organization: Rochester, MN

Contract Number: NO1-CB-43895
Starting Date: 6/15/74 Expiration Date: 2/28/78

Goal: (a) To determine values of never diagnostic tests in the detection of pancreatic cancer; (b) to determine whether surgical intervention of a localized pancreatic cancer significantly improves survival rate; and (c) to develop new procedures for pancreatic cancer diagnosis.

Approach: Three cooperating institutions will study, by a common protocol, patients who are suspicious of pancreatic cancer (PC) and warrant exploratory laparotomy. Tests to be done prior to surgery: CEA, alpha-fetoprotein and immunoglobulins, duodenal aspiration and study of pancreatic enzymes (PFT) and biliary secretion, ultrasonic abdominal study (U), fiberoptic duodenoscopy with retrograde pancreatocholangiography (RPCM), pancreatic scan with ^{75}Selenomethionine (S), selective celiac and/or superior mesenteric angiogram (A), and thermogram (T). At operation, portal blood will be obtained for additional studies. If pancreatic cancer is found at surgery, the patients will be evaluated at 3-month intervals for 3 years. If no cancer is found, patient will be evaluated at 6-month intervals for 3 years.

Progress: To date, 135 patients have been entered into the study. Analyses of the prospective comparison of current diagnostic tests on the first 70 patients surgically explored has now been completed. Pancreatic disease was detected in 90% of instances with pancreatic function tests and in 74% with ultrasound. Quantification of pancreatic CEA output did not differentiate all pancreatic cancer patients from other patients in any test condition. The pancreatic scan gave many false-positive results and thermography was insensitive. Arteriography, endoscopic retrograde pancreatography, and cytologic studies were 69%, 95%, and 23% accurate in diagnosis of pancreatic cancer. From these results, it is suggested that, when pancreatic cancer is suspected, abdominal ultrasound be given initially and if negative a pancreatic function test next. Positive results from either warrant endoscopic retrograde pancreatography for definitive diagnosis of pancreatic cancer. That sequence of tests in the present series identified 88% of patients without pancreatic disease and 89% with pancreatic cancer. Studies of various serum tumor markers were not helpful with the exception of CEA. The comparative value of computerized tomography to the above diagnostic tests are currently under evaluation.

Significance for Cancer Research (NCP Objective 5 Approach 3)

Project Officer: Louis P. Greenberg
Program: Diagnosis Site Visit Date: 3/21/77
Technical Review Group: Diagnostic Research Advisory Group
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: Usefulness of Carcinoembryonic Antigen in the Diagnosis of Bowel Cancer

Principal Investigator: Dr. Vay Liang W. Go
Name/Address Mayo Foundation
Performing Organization: Rochester, MN

Contract Number: NO1-CB-23854
Starting Date: 6/15/72 Expiration Date: 6/14/78

Goal: (a) Evaluate the CEA test in diagnosis of large bowel carcinoma; (b) continue evaluation of CEA as a biologic marker in patients undergoing chemotherapy, radiotherapy and immunotherapy of advanced gastrointestinal cancer; (c) measure CEA levels in blood and other specimens stored at NCI-Mayo Clinic Tumor Plasma Bank (CB-23879), Mayo Lung Cancer Project (NCI-CB-22000) and other contracts with the Immunodiagnosis Program of the Division of Cancer Biology and Diagnosis; (d) immunological quantification and chemical characterization of CEA-like material in secretions of the gastrointestinal tract; (e) continue to collect and provide colonic malignant tissue for different investigators in projects dealing with carcinoembryonic antigens.

Approach and Progress: (a) Results of serum CEA evaluation of 6,700 patients were previously reported. To date, follow-up information has been obtained on 531 normal subjects seen and followed over the past three years. None of the 15 normal subjects who had CEA > 5 ng/ml have developed detectable malignant neoplasms. Follow-up survival data of the patients who had colorectal cancer at the time of initial CEA determination have now been obtained. Among colorectal cancer patients with localized or with distant metastases involving the liver, those patients with an initial serum CEA < 5 ng/ml have a much better survival rate than patients with CEA > 5 ng/ml. (b) Serial determinations of serum CEA have been done on 612 patients with far advanced gastrointestinal malignancies who are currently being treated under various approved NCI protocols receiving chemotherapy, radiotherapy, and/or immunotherapy and 236 patients with colorectal cancer who were operated on with curative intent. Changes in CEA levels are currently being correlated with patient course, effect of cancer therapy, and relationship to other blood tests and measurable agents. (c) Immunochemical characterization of the CEA-like material from normal human colon washings shows it to be similar to tumor CEA.

Significance for Cancer Research (NCP Objective 5 Approach 3)

Project Officer: Louis P. Greenberg
Program: Diagnosis Site Visit Date: 2/9/77
Technical Review Group: Diagnostic Research Advisory Group
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $91,030

CONTRACT RESEARCH SUMMARY

Title: Detection of Small Amounts (over 7-10 ml/24 hours) of Human Blood in Human Feces

Principal Investigator:	Dr. Curtis L. Songster
Name/Address	University of Louisville Foundation, Inc.
Performing Organization:	Louisville, KY

Contract Number: NO1-CB-43968
Starting Date: 6/30/74 Expiration Date: 6/29/78

Goal: To generate a procedure that will detect small amounts of human blood (over 7-10 ml in 24 hours) in human fecal material by a simple, accurate (98%) examination.

Approach: The contractor shall develop a procedure for the detection of human blood in feces by utilizing antigens specific for the globin portion (alpha and beta chains) of hemoglobin. Application of the test will be made to an adequate number of persons both known to be bleeding and thought not to be bleeding; an adequate number of controls must have been on high meat, poultry, and fish diets and be truly negative by the proposed test.

Progress: High titer antisera have been raised against alpha and beta chains of human hemoglobin. Cow, pig, sheep, chicken, horse and fish hemoglobins lack cross-reaction. Cross-reactions with human hemoglobins are complete for A/A, A/S, A/C, S/S, S/C and monkey; partial with rabbit hemoglobin. Although native rabbit hemoglobin is weakly cross-reactive, heat-denatured rabbit hemoglobin (mimicking cooking of meat) is totally non-reactive.

Radial immunodiffusion techniques using anti-alpha-chain and anti-hemoglobin appear capable of specifically detecting human blood at levels of 2 mg% in purified A/A hemoglobin hemolysates. Fabricated fecal bleeds representing 3 to 100 milliliters of whole blood (assumed minimum hemoglobin levels of 10 grams/100 ml) can be routinely detected in 500 grams of stool sample thought to represent maximum fecal mass per 24-hour collection. Further antibody purification eliminated nonspecific precipitation. Various carriers and bacterial inhibitors have been employed to reduce bulk and contamination. Current studies are evaluating time, temperature, pH and bacterial flora effects upon the "antigen-carrier system." Test system components have a 90-day shelf life. Methods to increase sensitivity are being evaluated. Multiple specimen testing of preoperative patients with documented lesions is being studied to determine amount and frequency of bleeding, as well as locality of blood in the specimen.

Significance for Cancer Research (NCP Objective 5 Approach 3)

Project Officer: Louis P. Greenberg
Program: Diagnosis Site Visit Date: 4/13/76
Technical Review Group: Diagnostic Research Advisory Group
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $81,129

CONTRACT RESEARCH SUMMARY

Title: Screening Technique for Blood in Stool to Detect Early Cancer of Bowel

Principal Investigator: Name/Address Performing Organization:	Dr. Victor A. Gilbertsen University of Minnesota Minneapolis, MN

Contract Number: NO1-CB-53862
Starting Date: 6/30/75 Expiration Date: 6/29/78

Goal: The goal of this project is to demonstrate a significant reduction in mortality due to colorectal cancer between the annually screened and the control group by employing the Hemoccult (R) form of the guaiac test for stool blood in combination with a diagnostic protocol for the source of bleeding.

Approach: Forty five thousand participants between the ages of 50 and 80 years residing in the state of Minnesota are randomly allocated to three groups on the basis of age, sex, and geographic location in the state. Slides are completed after the observance of a meat-free diet with suggested high fiber content. One of the groups completes the slides once per year, another every other year, and a third group serves as the control. Participants submitting samples positive for blood receive a diagnostic examination (including a colonoscopy) to determine the cause of bleeding. All diagnostic procedures are conducted at the University of Minnesota Medical Center. All data including pathology reports on biopsy material and surgical specimens are computerized for easy retrieval. Extensive follow-up procedures are designed to retain participation of all subjects throughout the five years of testing and an additional five years of follow-up. Extensive dietary and health history data are collected from each subject via questionnaire.

Progress: Response rate after the first year of testing is 85% for test slides and 90+% for questionnaires (control group). Tested groups receive questionnaire at time of notification of negative slide results or at the time of diagnostic procedure should test be positive. Seventy-one percent of the 45,000 participants have been recruited as of May 1977.

Significance for Cancer Research (NCP Objective 5 Approach 3)

Project Officer: Louis P. Greenberg
Program: Diagnosis Site Visit Date: 4/20/76
Technical Review Group: Diagnosis Research Advisory Group
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $609,000

CONTRACT RESEARCH SUMMARY

Title: Early Detection of Ovarian Carcinoma in Asymptomatic Women

Principal Investigator: Dr. Malaya Bhattacharya
Name/Address Roswell Park Memorial Institute
Performing Organization: Buffalo, NY

Contract Number: NO1-CB-64013
Starting Date: 6/30/76 Expiration Date: 6/29/79

Goal: The goal of this project is the development of sensitive immunoassay procedures for early diagnosis of ovarian cancers and serial monitoring of patients undergoing therapy for ovarian cancers.

Approach: The investigation will be conducted on the following topics: (1) preparation of antisera (anticystadenocarcinoma sera); (2) sources of ovarian cystadenocarcinoma-associated antigens (OCAA); (3) purification of OCAA by conventional methods, immunoadsorbent columns, affinity columns of plant lectins, (4) determination of purity of OCAA; (5) characterization of OCAA; (6) determination of the frequency of occurrence of OCAA in other cancer and non-cancer tissues; (7) development of a radioimmunoassay for detection of OCAA; (8) patient selection, availability and follow-up; (9) characterization of immune response to ovarian cancers with emphasis on cystadenocarcinoma; and (10) problems and limitations of the proposed projects.

Progress: Evidence has been found for the presence of at least three different tumor-associated antigens or antigenic determinants in human cystadenocarcinomas of the ovary. Solid ovarian tumors, tumor cells in ascites fluids and cyst fluids from ovarian cancer patients were used as sources for these antigens. Antisera were raised in rabbits against cystadenocarcinoma extracts. After proper adsorptions the antisera produced were used to perform the assays for tumor-associated antigenic reactivity. For quantitative isolation of these antigens repeated extractions separately or in combinations with 3M KCl, 6M urea and normal saline were performed; 3 time extraction with saline gave the best results. Ammonium sulfate fractionation of the saline extracts gave about six- to ten-fold purification. Further fractionation of the saline extracts gave about six- to ten-fold purification. Further fractionation by gel filtration and ion-exchange chromatography has yielded about 120-fold purification of the antigens. Antisera now are being produced in rabbits against these preparations. Further purification of the antigens utilizing immunoadsorbent columns and affinity columns are under way.

Significance for Cancer Research (NCP Objective 5 Approach 3)

Project Officer: Louis P. Greenberg
Program: Diagnosis Site Visit Date: 12/14/76
Technical Review Group: Diagnostic Research Advisory Group
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $55,453

CONTRACT RESEARCH SUMMARY

Title: Early Detection of Ovarian Carcinoma in Asymptomatic Women

Principal Investigator: Name/Address Performing Organization:	Dr. Leo Stolbach Tufts University School of Medicine Boston, MA

Contract Number: N01-CB-64028
Starting Date: 6/30/76 Expiration Date: 6/29/79

Goal: The goal of this project is to develop a screening test for the early diagnosis of ovarian carcinoma in asymptomatic women.

Approach: Malignant effusion of patients with ovarian carcinoma will be processed in order to (1) isolate and purify tumor-specific antibodies and/or antibody-antigen complexes from effusion fluids; (2) dissociate the antibody-antigen complexes and separate the tumor-associated antigens and antibodies making up these complexes; (3) determine the immune specificity of antibodies isolated from the effusion fluids; (4) detect tumor-associated antigen in the effusion fluid and tumor extracts; (5) ulize the tumor-specific antibodies to prepare an immunoadsorbent for the purification of the antigen; and antibodies to prepare an immunoadsorbent for the purification of the antigen; and (6) develop a diagnostic assay for detecting circulating antibody, antigen and antigen-antibody complexes in patients with various stages of ovarian malignancy.

Progress: Antibodies have been isolated from the effusion fluids of 38 patients with ovarian carcinoma. These antibodies have been absorbed with a polymer of normal ovaries and plasma, and tested for titer and specificity by indirect immunofluorescence (IF) against cells obtained from malignant effusions from ovarian and control cancer patients. Antibodies from 6 patients have shown specificity for ovarian cancer cells. Three approaches are being used to isolate an ovarian-associated antigen: (1) High titer absorbed ovarian antibodies coupled to Sepharose 4B have been used to isolate minute amounts of material from tumor extracts. (2) Preliminary results using Clq to test for immune complexes indicate that some of the fluids and also the antibodies isolated from them contain Clq-positive material. (3) Isolated IF-negative antibodies and/or complexes, when subjected to low pH gel chromatography or rapid neutralization and ion-exchange chromatography, have yielded antibodies which give positive results when tested by indirect IF against ovarian cancer cells. Material obtained by these approaches is presently being investigated for the presence of an ovarian-associated antigen(s).

Significance for Cancer Research (NCP Objective 5 Approach 3)

Project Officer: Louis P. Greenberg
Program: Diagnosis Site Visit Date: 12/13/76
Technical Review Group: Diagnostic Research Advisory Group
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 76 Funds: $95,426 (TQ)

CONTRACT RESEARCH SUMMARY

Title: Hormone Markers for the Detection and Diagnosis of Cancer

Principal Investigator: Name/Address Performing Organization:	Dr. William D. Odell Harbor General Hospital Torrance, CA

Contract Number: N01-CB-43903
Starting Date: 6/1/74 Expiration Date: 5/31/78

Goal: To develop hormone markers that might indicate the presence of small (early), treatable cancer.

Approach: (1) To measure ADH, vasotocin, oxytocin, α and β MSH, ACTH, α and β TSH, and α and β HCG to search for tumor elaboration of these peptides among cancer patients; (2) to develop new techniques for separating and identifying "prohormone" forms of ACTH, gastrin, and pancreozymin-cholecystokinin (PZ-CCK); (3) to search for the existence of such big forms of ADH, oxytocin, α and β MSH, luteinizing hormone, and α and β glycopeptides, (4) to develop peptide assays for fetal hormones related to vasopressin; and (5) to identify other nonhormonal peptides which might be used as cancer markers. The contractor hypothesized that "ectopic peptide elaboration is a universal concomitant of neoplasia." This hypothesis is based on a review of several hormonal syndromes produced by nonendocrine cancers and the fact that, where known, they are produced by peptides. Production of nonbiologically active peptides is even more common than production of active peptides.

Progress: The elaboration of several peptides by several common cancers (lung, colon, breast, and prostate) has been investigated. In addition, smaller numbers of less common cancers have been studied. For each tumor type, the usefulness of six peptides (big- or pro-ACTH, β lipotropin, alpha chain of glycopeptides, beta chain, HCG, vasopressin-vasotocin, and a PTH-related peptide) with weak biological activity as tumor markers has been evaluated.

Results indicate that the hypothesis is valid. Over 95% of 87 tumor extracts contained greater amounts of these peptides than blood concentration. In a prospective blind study of patients with abnormal chest x-rays, 83% of those subjects shown to have lung cancers had elevations of one or more of these peptides. The following elevated levels were found in the blood plasma of lung cancer patients: ACTH-72%; BLPH-62%; α-chain, men-11%; α-chain, women-6%; β chain-7%; AVP/AVT-41%. Similar studies are nearly completed for colon cancer, and are in progress for breast cancer.

Significance for Cancer Research (NCP Objective 5 Approach 4)

Project Officer: Louis P. Greenberg
Program: Diagnosis Site Visit Date: 3/14/77
Technical Review Group: Diagnostic Research Advisory Group
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $230,402

CONTRACT RESEARCH SUMMARY

Title: Biochemical Markers or Enzyme Changes That May Presage the Presence of Cancer

Principal Investigator:	Dr. Alexander Brownie
Name/Address	State University of New York
Performing Organization:	Buffalo, NY

Contract Number: NO1-CB-43977
Starting Date: 6/1/74 Expiration Date: 12/31/77

Goal: To develop and establish a highly sensitive test for a specifically prostatic form of serum acid phosphatase as a marker for early prostatic cancer.

Approach: It is intended to prepare in bulk the isoenzymes of human prostatic acid phosphatase, by methods previously proven in this laboratory. Both the water-extracted types, which are believed to be secreted in the prostatic fluid, and the detergent-extracted type (obtained by a Tween method) will be examined separately. Each will be used as an antigen to obtain antibody and other reagents for a radioimmunoassay method, for its specific detection at very low levels in sera. Each will also be studied for any specific binding or inhibitory property that can characterize it at low levels in the presence of other phosphatases.

Progress: The acid phosphatase from cancerous human prostatic tissue was purified and a rabbit antiserum to this purified enzyme was prepared. The antiserum is specific for the prostate enzyme; it did not cross react with acid phosphatases from other human tissues, such as kidney, liver, lung, spleen, red blood cells, etc. With this purified enzyme and its antiserum, a sensitive and specific immunochemical method has been developed, which detects as low as 0.2-0.4 IU or 10-20 ng/ml of prostatic acid phosphatase. With this method it was possible to detect 20% of stage B, 50% of stage C and 80% of stage D prostate cancers. The isoenzymes of human prostatic acid phosphatase were studied by an isoelectric focusing technique. Purified acid phosphatase from malignant prostatic tissues contained eight distinct isoenzymes with pI 4.7-5.3. The sera from patients with prostatic cancer were shown to have similar acid phosphatase isoenzymes. Serum RNase activities were also found to be significantly increased in patients with prostatic cancer when compared with those in normal healthy individuals.

Significance for Cancer Research (NCP Objective 5 Approach 4)

Project Officer: Louis P. Greenberg
Program: Diagnosis Site Visit Date: 3/17/75
Technical Review Group: Diagnostic Research Advisory Group
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: Development and Serum Isozyme Test for Human Cancer Patients

Principal Investigator: Dr. K. C. Tsou
Name/Address University of Pennsylvania
Performing Organization: Philadelphia, PA

Contract Number: NOI-CB-64029
Starting Date: 6/30/76 Expiration Date: 4/30/79

Goal: To improve on the early diagnosis of cancer of the liver and further examine the possibilities of preventing the spread of primary cancers to other body sites with concentration on liver tissue.

Approach: The project involves: (1) further technical improvement of the 5'-nucleotide phosphodiesterase isozyme method by gel electrophoresis as a diagnostic tool; (2) further development of correlation data (biopsy, scan) and 5'-nucleotide phosphodiesterase-V for primary hepatoma; (3) further definition of possible relationships of the isozyme band V of this enzyme to liver metastasis; (4) investigation of possible relationships between this isozyme and other known liver markers related to hepatic cancer, especially α-fetoprotein and hepatitis B surface antigen (Australia antigen); (5) improvement of sensitivity of the test through development of an alternate assay method, including immunoassay if an antienzyme antibody can be prepared with reasonable ease; (6) correlation of clinical information and other liver function tests with the results of this test; and (7) protocol for the use of this test in development of an early diagnosis.

Progress: Out of 21 cases of biopsy proven primary hepatomas, 20 cases are positive for 5'-nucleotide phosphodiesterase isozyme-V (95%). Of this group, only 5 have α-fetoprotein level > 40 ng/ml. The one single case is negative for the isozyme and < 10 ng/ml for αFP. In the group of patients with known liver metastasis by biopsy or scan, 52 out of 54 samples are positive (96.47%). In the group of patients with no known liver metastasis at the time of sampling by either liver scan or clinical symptoms, 74/229 patients are positive (32.3%). Follow-up of 11 patients in this group showed that eight did have metastasis to the liver in their autopsy record.

This isozyme has also been found in active hepatitis B and disappears when the patient recovers. Australian antigen-positive carriers are, however, negative with respect to this isozyme.

Significance for Cancer Research (NCP Objective 5 Approach 3)

Project Officer: Louis P. Greenberg
Program: Diagnosis Site Visit Date: 3/4/77
Technical Review Group: Diagnostic Research Advisory Group
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $110,043

CONTRACT RESEARCH SUMMARY

Title: Study of a Serum Alkaline Phosphatase Variant in Cancer Patients

Principal Investigator: Name/Address Performing Organization:	Dr. Frank C. Larson University of Wisconsin School of Medicine Madison, WI

Contract Number: NO1-CB-74173
Starting Date: 9/15/77 Expiration Date: 9/14/78

Goal: To define more clearly the possible diagnostic significance of the presence of an isoenzyme of alkaline phosphatase in serum of human cancer patients.

Approach: First, to screen a sufficient number of patients with a variety of cancers to determine whether the elevation in serum alkaline phosphatase variant (APV) found in preliminary studies is characteristic of all cancer types or restricted to cancers of certain organ sites and cell types. Next, to make sequential measurements in patients with cancer types which are found to be associated with APV to ascertain if variations in levels of serum APV reflect changes in cancer load following surgery, radiotherapy, or chemotherapy. Finally, to test effect of method improvement on discriminating power of the APV assay.

Progress: New Contract

Significance for Cancer Research (NCP Objective 5 Approach 4)

Project Officer: Louis P. Greenberg
Program: Diagnosis
Technical Review Group: Diagnostic Research Advisory Group
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $54,000

CONTRACT RESEARCH SUMMARY

Title: Determination of Optimal Frequency of Screening Strategies

Principal Investigator: Name/Address Performing Organization:	Dr. Arthur Albert Boston University Boston, MA

Contract Number: N01-CB-53863
Starting Date: 6/1/75 Expiration Date: 8/31/77

Goal: To develop a means whereby the optimum frequency of screening can be determined for early cancer for various anatomic sites in order to assure success in such screening at the least possible cost and hazard to the patient and still be effective in reducing death from cancer.

Approach: A team of clinicians, pathologists, statisticians, operations researchers and epidemiologists will carry out extensive investigation and documentation of the level of present knowledge, both empirical and theoretical on the following five factors: (1) the natural history or development of the disease, (2) the incidence of the disease in the target population; (3) the effectiveness (sensitivity and specificity) of the various available screening tests at each stage of the disease; (4) the effectiveness (on mortality) of intervention (treatment during each stage of the disease); and (5) the cost and hazards of the various screening tests. Disease models will be developed and validated for which screening data exist, or must be developed, such as colon, lung, bladder and prostatic cancer. Through parametric analysis these models will be used to suggest general ranges or minimum limits on the performance of screening tests if they are to be effective in early cancer detection and reducing cancer mortality.

Progress: Accomplishments during this 2-year contract include the following: (1) Development of a time-dynamic model: The joint frequency of age and natural history sojourn times represent a statistical picture of the disease natural history in the population. (2) Development of optimum individual screening policies: Exercising this model has allowed evaluation of the objective function for any specified policy or search for an optimal policy. (3) Development of an urn model for the natural history of cancer in a population at an instant of time: This model allows for calculation of temporal changes in prevalences, incidences and epidemiologic descriptors. (4) Development of estimation techniques for determining statistical properties of the disease natural history in a population: This allows for accurate determination of occurrence rates of non-observable events such as the age-specific incidence of preclinical disease.

Significance for Cancer Research (NCP Objective 5 Approach 3)

Project Officer: Louis P. Greenberg
Program: Diagnosis Site Visit Date: 5/3/76
Technical Review Group: Diagnostic Research Advisory Group
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $7,700

CONTRACT RESEARCH SUMMARY

Title: Determination of Optimal Frequency of Screening Strategies

Principal Investigator: Name/Address Performing Organization:	Dr. Michael J. Brennan Michigan Cancer Foundation Detroit, MI

Contract Number: NO1-CB-53907
Starting Date: 6/1/75 Expiration Date: 8/31/77

Goal: To develop a means whereby the optimal frequency of screening can be determined for early cancer of various anatomic sites in order to assure success in such screening at the least possible cost and hazard to the patient and still be effective in reducing death from cancer.

Approach: A team of clinicians, pathologists, statisticians, operations researchers and epidemiologists will carry out extensive investigation and documentation of the level of present knowledge, both empirical and theoretical on the following five factors: (1) the natural history of development of the disease; (2) the incidence of the disease in the target population; (3) the effectiveness (sensitivity and specificity) of the various available screening tests at each stage of the disease; (4) the impact (on mortality) of intervention (treatment during each stage of the disease); and (5) the cost and hazards of the various screening tests. Disease models will be developed and assessed for sites on which screening data already exist, such as colon, breast and cervical cancer. Lung, bladder and prostatic cancer models will also be undertaken to help define the requisite characteristics of screening techniques for these diseases. Through appropriate statistical and mathematical methods these models will be used to suggest general ranges or minimum limits on the performance of screening tests if they are to be effective in early cancer detection and reducing cancer mortality.

Progress: The models of breast, cervical, and colorectal cancer have been modified and extended. This work has been based on the feedback received in the preliminary analysis phase of the project completed in the first year. A Semi-Markov model has been developed that incorporates the underlying principles of the site-specific analyses. A decision theoretic framework has been used to analyze the number of tests to be given and the decision rules to be followed at a given screening examination. Finally, literature on lung and prostate cancer has been reviewed as a basis for formulating the analyses for these sites.

Significance for Cancer Research (NCP Objective 5 Approach 4)

Project Officer: Louis P. Greenberg
Program: Diagnosis Site Visit Date: 5/3/76
Technical Review Group: Diagnostic Research Advisory Group
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $7,600

CONTRACT RESEARCH SUMMARY

Title: Experiment to Assess the Impact of Multi-site Screening on Total Cancer Mortality

Principal Investigator:	Dr. Dean F. Davies
Name/Address	University of Tennessee
Performing Organization:	Memphis, TN

Contract Number: N01-CB-53864
Starting Date: 6/23/75 Expiration Date: 12/22/77

Goal: The goal of this project is to achieve a design that can be put to clinical use in order to effectively reduce cancer mortality.

Approach: A team has been established with expertise in the fields of clinical oncology, radiology, epidemiology, and statistics. The experimental design will be developed on the basis of available knowledge of (1) high-risk factors, (2) quality of screening procedures, (3) variability in the effectiveness of present day treatment, (4) cost, (5) compliance with follow-up examinations and follow through procedures, (6) side effects of treatments, (7) incidence rates, (8) prevalence rates, and (9) case fatality rates. The rationale for the experimental design will be expressed in a format which makes explicit the use of available information and accepted assumptions.

Progress: A randomized experiment has been designed for determining the effectiveness and the cost-benefit of multi-layered screening for lung, breast, colon/rectum, cervical and endometrial cancers. For this purpose a simulation model has been constructed and tested, and the optimum age groups, optimum risk levels, markers, and end-points have been specified.

By judicious prescreening by questionnaire the composite risk levels that are necessary to exclude the low-risk populations and to obtain a more cost-effective experiment using relatively high yield populations is possible. The experiment would test the validity and precision of the risk level estimates.

Acquisition of cost estimates and completion of the protocol of the design should be completed within the next year. Pretesting of selected "nodes" of the Flow Tree Diagram is indicated for a reliable estimate of the magnitude and cost of the experiment.

Significance for Cancer Research (NCP Objective 5 Approach 3)

Project Officer: Louis P. Greenberg
Program: Diagnosis Site Visit Date: 5/4/76
Technical Review Group: Diagnostic Research Advisory Group
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: Breast Diagnosis: Quantitative Imaging by Ultrasound

Principal Investigator:	Dr. James F. Greenleaf
Name/Address	Mayo Foundation
Performing Organization:	Rochester, MN

Contract Number: NO1-CB-64041
Starting Date: 6/30/76 Expiration Date: 6/29/78

Goal: To determine if images representing quantitative distribution of basic mechanical tissue properties or acoustic parameters of tissue such as velocity, attenuation, reflection, impedance and scattering can be useful in breast cancer diagnosis and of more value than images representing tissue interfaces and geometries such as B-scans.

Approach: A transverse radial scanning system has been designed and constructed which acquires ultrasound data from excised tissues and patients in several modes including echos for compound B-scans, time-of-flight and attenuation data for mathematical reconstruction. The ability of acoustic tissue characterization to detect and distinguish excised normal and diseased tissues is being studied by comparing results from visual evaluation and computer-aided feature extraction and pattern recognition of the various acoustic images with computer encoded histologic characteristics obtained from microscopic evaluation of tissue sections removed from the intact organ. Initial studies have begun of normal and diseased breasts in vivo in selected patients and the resulting acoustic images are being compared to histology obtained from breasts of those women who undergo mastectomy.

Progress: Signal preprocessing systems and scanner control electronics have been designed and constructed. Software programs for data acquisition analysis and display are being written and documented. Temperature dependence of acoustic speed in various tissue components of breast tissue is being studied. Protocols for acquisition of patient data and subsequent tissue analysis are being developed. The first patients have been scanned.

Significance for Cancer Research (NCP Objective 5 Approach 5.4)

Project Officer: Bernice T. Radovich, Ph.D., R. Quentin Blackwell, Ph.D.
Program: Breast Cancer Diagnosis
Technical Review Group: Diagnostic Radiology Committee
Relevance Review Group: Breast Cancer Steering Committee
FY 77 Funds: $137,000

CONTRACT RESEARCH SUMMARY

Title: Breast Cancer Tissue Supply

Principal Investigator: Name/Address Performing Organization:	Dr. Paul H. O'Brien Medical University of South Carolina Charleston, SC

Contract Number: N01-CB-23867
Starting Date: 6/30/72 Expiration Date: 6/29/78

Goal: To obtain tissue and blood specimens from patients with breast cancer for use in immunodiagnostic assays.

Approach: At the time of surgery, obtain tumor and normal breast tissue. Obtain serum and peripheral blood lymphocytes before surgical therapy and at regular intervals thereafter. These specimens are shipped promptly to other investigators in the program for use in immunodiagnostic assays.

Progress: During the period from August 1, 1976 to April 30, 1977, there were approximately 34 preoperative blood specimens from patients with malignant breast tumors, 34 malignant breast tumors, 85 blood samples from patients with benign breast diseases, 54 follow-up blood specimens on patients with malignant tumors, and 149 blood samples sent for special studies on patients with breast cancer. There were 5 benign breast tumor samples sent during this period of time. Benign blood samples and tumors were shipped only upon request.

Significance for Cancer Research (NCP Objective 5 Approach 5.4)

Project Officer: Ronald B. Herberman, M.D.
Program: Breast Cancer Diagnosis
Technical Review Group: Breast Cancer Diagnosis Committee
Relevance Review Group: Breast Cancer Steering Committee
FY 77 Funds: $55,000

CONTRACT RESEARCH SUMMARY

Title: Immunological Studies of Human Mammary Carcinoma

Principal Investigator: Dr. Donald M. Marcus
Name/Address: Albert Einstein College of Medicine
Performing Organization: Bronx, NY

Contract Number: NO1-CB-23871
Starting Date: 6/20/72 Expiration Date: 6/19/78

Goal: (1) To identify antigens associated with breast cancer and to develop a quantitative radioimmunoassay (RIA) for use in immunodiagnosis of breast cancer; and (2) to study the correlation between in vitro assays for cell-mediated immunity to breast tumors and the clinical status and course of patients, and to identify antigens that elicit cellular immunity.

Approach: (1) To develop antisera specific for tumor-associated antigens, purify the antigens by immunoadsorbent and biochemical techniques and to use the purified antigens in a double-antibody RIA. (2) To make extracts of primary breast tumors obtained at the time of surgical resection and to test autologous and allogeneic extracts against the lymphocytes of the patient by three assays:—(a) a viral plaque assay developed by Dr. B. Bloom; (b) inhibition of leukocyte migration; and (c) incorporation of ^{3}H-thymidine.

Progress: (1) Serum ferritin values are elevated in many patients with breast cancer. The contractor is collaborating with the NCI in evaluating ferritin and other markers in the immunodiagnosis of breast cancer, and recently assayed approximately 750 coded sera. The statistical analysis is not complete, but the combination of ferritin and CEA appears to be very promising. Acidic isoferritins have antigenic determinants that differ from normal adult liver and spleen ferritins. An RIA for acidic isoferritins was devised to determine if this assay detects cases of breast cancer that are not detected by our standard ferritin RIA.

Significance for Cancer Research (NCP Objective 5 Approach 5.4)

Project Officer: K. Robert McIntire, M.D., Bernice T. Radovich, Ph.D.
Program: Breast Cancer Diagnosis Site Visit Date: 2/5/76
Technical Review Group: Breast Cancer Diagnosis Committee
Relevance Review Group: Breast Cancer Steering Committee
FY 77 Funds: $110,738

CONTRACT RESEARCH SUMMARY

Title: Immunologic Cross Reactions Between Breast Cancer and Mammary Tumor Virus

Principal Investigator:	Dr. Grace B. Cannon
Name/Address	Litton Bionetics, Inc.
Performing Organization:	Kensington, MD

Contract Number: N01-CB-74087
Starting Date: 7/1/77 Expiration Date: 6/30/78

Goal: To perform the leukocyte migration inhibition (LMI) assay for the detection of mouse mammary tumor virus (MMTV) and associated (gp-52) antigens to ascertain the usefulness of CMI assays for the early diagnosis, monitoring and prognostic predictability of breast cancer.

Approach: Breast cancer patients (prior to biopsy and post mastectomy), benign disease patients (pre and post biopsy), patients with other types of cancers, patients with gynecological disease and healthy female controls will be tested under code with MMTV and gp-52. Antigen controls will be gp-70, other coded glycoproteins, glycoprotein subunits, a 3M KCl extract of MCF-7 and an extract of a lymphocyte pool from several normal individuals, and mumps antigen.

Progress: New Contract

Significance for Cancer Research (NCP Objective 5 Approach 5.4)

Project Officer: Bernice T. Radovich, Ph.D.
Program: Breast Cancer Diagnosis Site Visit Date: 1/11/77
Technical Review Group: Breast Cancer Diagnosis Committee
Relevance Review Group: Breast Cancer Task Force Steering Committee
FY 77 Funds: $118,337

CONTRACT RESEARCH SUMMARY

Title: Pathology Laboratory for Cooperative Clinical Studies

Principal Investigator:	Dr. Gilbert H. Friedell
Name/Address	St. Vincent Hospital
Performing Organization:	Worcester, MA

Contract Number: N01-CB-80704
Starting Date: 3/18/68 Expiration Date: 4/17/78

Goal: To identify and define pathologic prognostic features in cases accessioned in the Primary Therapy of Breast Cancer Study; to study these features in comparable pathologic material from British, Japanese, and Hawaiian-Japanese breast cancer patients; and to correlate this information with clinical and other laboratory data from these cases.

Approach: The pathologic material collected at the Central Pathology Laboratory from the Collaborating Clinical Centers, and that subsequently received from British, Japanese, and Hawaiian-Japanese sources, has been--and is being--reviewed without knowledge of the clinical findings or other laboratory data, after which the correlations are carried out. Subsequent to the initial correlative efforts, the pathologic material is--and will be--reviewed again in an attempt to pinpoint findings of particular importance.

Progress: The tumor type and grade, nuclear grade, and presence of blood vessel invasion at the primary tumor site, and the presence of regional lymph node involvement have been determined in 381 cases and a report defining the study has been published. A report of some clinico-pathologic correlations was presented at the May 1977 ASCO meeting in Denver and a manuscript has been submitted for publication. A workshop on sinus histiocytosis utilizing material from the Central Pathology Laboratory was carried out and a report has been submitted for publication. A review of sinus histiocytosis in the 381 cases is in progress. A joint review with other pathologists of sinus histiocytosis in axillary lymph nodes from Japanese, Hawaiian-Japanese, and British breast cancer patients has been completed and a manuscript is in preparation. A detailed review of all axillary lymph nodes in radical mastectomy specimens from Japanese patients treated five or more years at the National Cancer Center Hospital in Tokyo is almost completed.

Significance for Cancer Research (NCP Objective 5 Approach 5.4)

Project Officer: Ihor J. Masnyk, Ph.D.
Program: Breast Cancer Diagnosis
Technical Review Group: Breast Cancer Diagnosis Committee
Relevance Review Group: Breast Cancer Steering Committee
FY 77 Funds: 0 (No Cost Extension)

CONTRACT RESEARCH SUMMARY

Title: NCI Sera Bank Facility for the Breast Cancer Task Force

Principal Investigator:	Dr. Alan Schutt
Name/Address	Mayo Foundation
Performing Organization:	Rochester, MN

Contract Number: NO1-CB-23879b
Starting Date: 9/1/77 Expiration Date: 8/31/78

Goal: To establish and maintain a storage facility for serum specimens to be used by the Breast Cancer Task Force in a program designed to search for biological markers in breast cancer.

Approach: Sera specimens will be secured from breast cancer patients, benign disease patients, controls and from a screening population, under separate contracts setting up a patient resource. The material will be processed, recorded and stored in -70°C deep freezers under easily retrievable conditions with all clinical data available. It will be used in the search for and verification of new breast cancer markers.

Progress: New Contract

Significance for Cancer Research (NCP Objective 5 Approach 5.4)

Project Officer: Ihor J. Masnyk, Ph.D., Bernice T. Radovich, Ph.D.
Program: Breast Cancer Diagnosis
Technical Review Group: Breast Cancer Biological Markers Group
Relevance Review Group: Breast Cancer Steering Committee
FY 77 Funds: $91,600

CONTRACT RESEARCH SUMMARY

Title: Prognostic Factors for Disseminated Cancer in Patients with Early Breast Cancer

Principal Investigator: Dr. Paul Peter Rosen
Name/Address Memorial Hospital
Performing Organization: New York, NY

Contract Number: N01-CB-74097
Starting Date: 8/1/77 Expiration Date: 7/31/78

Goal: To determine the frequency of subsequent metastatic breast cancer in a group of females with "early" invasive carcinoma and to identify those clinical and/or pathologic features or groups of features that are indicators of a high or low risk for dissemination of carcinoma.

Approach: A study population of 250 women with primary infiltrating breast carcinomas 1.0-2.0 cm in diameter, also a subset of 100 women with malignant tumors 1 cm or less in diameter will be identified in a retrospective study (1960-1968) and followed for at least 10 years. These patients will have been treated by at least a modified radical mastectomy and been found to have negative lymph nodes. The relationships observed between pathologic and clinical data and survival will be evaluated in order to identify those factors associated with a high and low frequency of recurrence.

Progress: New Contract

Significance for Cancer Research (NCP Objective 5 Approach 5.4)

Project Officer: Bernice T. Radovich, Ph.D.
Program: Breast Cancer Diagnosis Site Visit Date: 4/12/77
Technical Review Group: Breast Cancer Diagnosis Committee
Relevance Review Group: Breast Cancer Task Force Steering Committee
FY 77 Funds: $70,031

CONTRACT RESEARCH SUMMARY

Title: Biochemical Analysis of Human Breast Cyst Fluid (BCF)

Principal Investigator: Dr. Morton K. Schwartz
Name/Address Sloan-Kettering Institute for
Performing Organization: Cancer Research
New York, NY

Contract Number: NO1-CB-53853
Starting Date: 6/30/75 Expiration Date: 9/14/78

Goal: To establish the biochemical and immunochemical composition of human BCF; to search for a marker which might be useful in understanding the formation of cysts, their treatment, and the risk of patients with cysts to develop cancer.

Approach: BCF from patients with cystic mastopathy will be analyzed for polypeptide and steroid hormones, tumor-associated antigens, enzymes, lipids, minerals and trace elements. These data will be correlated with each other and with the demographic information. Fluid will be analyzed from patients with recurrent cysts and clinical follow-up will be obtained on all patients.

Progress: As of March 23, 1977, detailed analysis had been carried out on BCF from 589 patients. Seventy-two of these patients have had recurrent cysts and additional specimens submitted for analysis since their initial aspiration. As previously noted, the concentrations in many BCF specimens of CEA, α-fetoprotein, β-subunit hCG, calcium, copper, zinc, total protein, albumin, cholesterol, phosphohexose isomerase, γ-glutamyl transpeptidase, β-glucuronidase, lactic dehydrogenase, amylase, dehydroisoandrosterone, androsterose, and their sulfates are many fold the concentrations of these constituents found in serum. Correlation of BCF concentrations for many of these constituents between patients were found to be significant. The specimen variation was much less in specimens from the same patient obtained either at the same time or on subsequent aspiration than that from patient to patient. Notwithstanding the large BCF to serum gradient, isotope studies have indicated a slow influx and efflux of the steroids into the cyst fluid. The fluid appears to contain material both of a secretory nature and that resulting from cell breakdown.

Significance for Cancer Research (NCP Objective 5 Approach 5.4)

Project Officer; Bernice T. Radovich, Ph.D., R. Quentin Blackwell, Ph.D.
Program: Breast Cancer Diagnosis Site Visit Date: 5/5/77
Technical Review Group: Breast Cancer Diagnosis Committee
Relevance Review Group: Breast Cancer Steering Committee
FY 77 Funds: $98,060

CONTRACT RESEARCH SUMMARY

Title: Evaluation of Serum LDH Isoenzymes in Women with Breast Tumors

Principal Investigator: Name/Address Performing Organization:	Dr. Ervin J. Havrylewicz Mercy Hospital and Medical Center Chicago, IL

Contract Number: NO1-CB-53855
Starting Date: 6/30/75 Expiration Date: 9/14/78

Goal: To determine if a highly reproducible LDH isoenzyme test can be utilized as a diagnostic marker for breast cancer.

Approach: Blood will be drawn on 800 patients with breast disease, including malignant and benign tumors, and patients with other gynecological problems. Emphasis will be placed on securing serum samples prior to surgery. Patient cooperation will be requested when presenting for mammographic examination, and when available, LDH isoenzyme patterns will be correlated with the mammogram report. Longitudinal sampling following the course of disease will be pursued. In addition to these patients, blood from 200 women clinically free of breast disease will be obtained as control. All samples will be coded immediately; laboratory personnel will not have access to the code. Serum LDH isoenzyme patterns will be resolved, evaluated and classified as Ca Type or N Type (normal), the latter including normal, benign breast tumor, breast cancer in remission (post-surgical). After submission of evaluations, the data will be compared with the tumor classification to assess the correctness of diagnosis and to determine if other correlations can be made with relationship to nodal involvement, metastases, cell type, etc.

Progress: In excess of 950 blood samples have been collected and electrophoresed and densitometry completed. All samples are processed minimally as duplicate determinations utilizing 10 µl serum. Based on currently established criteria, preliminary diagnosis on 850 samples has been completed and correlated with the pathology diagnosis. These data indicate the following correct correlations: normals 79%; dysplasia, etc. 70%; fibroadenoma 74%; fibrocystic disease 68%; and pre-surgical carcinoma 70%. Sixty-seven postoperative serum samples were obtained in the acquisition group, 201-700. Of this number, 51 patients had no evidence of disease clinically and 42 patients were reported LDH negative; correlation value 83%. Of the remaining 16 clinically positive patients, 11 patients exhibited positive LDH patterns; correlation value 69%. Mammographic diagnosis is correlated at a level of 85%.

Significance for Cancer Research (NCP Objective 5 Approach 5.4)

Project Officer: Ronald B. Herberman, M.D., Bernice T. Radovich, Ph.D.
Program: Breast Cancer Diagnosis Site Visit Date: 10/26/76
Technical Review Group: Breast Cancer Diagnosis Committee
Relevance Review Group: Breast Cancer Steering Committee
FY 77 Funds: $34,440

CONTRACT RESEARCH SUMMARY

Title: Longitudinal Studies of Biologic Markers in Breast Cancer Patients

Principal Investigator: Name/Address Performing Organization:	Dr. Howard H. Sussman Stanford University Medical Center Stanford, CA

Contract Number: N01-CB-74086
Starting Date: 8/1/77 Expiration Date: 7/31/78

Goal: To assay human breast cancer tissue and sera prior to mastectomy and throughout the clinical course of the disease for potential markers to determine how effective such markers would be for early detection of breast cancer and its recurrence and to gain an understanding of the relationship between the concentration of the marker substances in the individual tumor and in the serum levels of the host.

Approach: Tumor and sera of patients presenting initially for diagnosis and primary therapy (category 1) will be assayed for the fetoplacental proteins, i.e., placental alkaline phosphatase (PAP), human chorionic gonadotropin (hCG) α and β, human placental lactogen (hPL) and carcinoembryonic antigen (CEA), and tests on sera will be repeated sequentially every three months. Patients developing recurrences (categories 2 and 3) will be included with a study population from the Northern California Oncology Group. Another objective of the study will be to identify new ectopically synthesized placental membrane proteins which may be common to both trophoblasts and neoplastic breast tumor cells.

Progress: New Contract

Significance for Cancer Research (NCP Objective 5 Approach 5.4)

Project Officer: Bernice T. Radovich, Ph.D.
Program: Breast Cancer Diagnosis Site Visit Date: 4/4/77
Technical Review Group: Breast Cancer Diagnosis Committee
Relevance Review Group: Breast Cancer Task Force Steering Committee
FY 77 Funds: $111,650

CONTRACT RESEARCH SUMMARY

Title: Longitudinal Studies of Biologic Markers in Breast Cancer Patients

Principal Investigator: Dr. Morton K. Schwartz
Name/Address Sloan-Kettering Institute for Cancer
Performing Organization: Research
New York, NY

Contract Number: NO1-CB-74206
Starting Date: 8/1/77 Expiration Date: 7/31/78

Goal: To assay human breast cancer tissue and sera prior to mastectomy and throughout the clinical course of the disease for potential markers to determine how effective such markers would be for early detection of breast cancer and its recurrence and to gain an understanding of the relationship between the concentration of the marker substances in the individual tumor and in the serum levels of the host.

Approach: Serum and tissue specimens from patients entering for diagnosis and for primary therapy will be assayed for carcinoembryonic antigen (CEA), sialytransferase, phosphohexose isomerase (PHI) and spermine, ferritin, lactic dehydrogenase (LDH) and its isoenzymes, glucose-6-phosphate dehydrogenase (G6PD)-tissue only as a reference, β-hCG, γ-glutamyltranspeptidase and α-fetoprotein and IgA. Total protein and DNA will also be determined to serve as points of reference. Sera specimens will be collected prior to surgery, before discharge and then sequentially, every three months the first year and every six months thereafter. For those with no recurrences, specimens will be collected on a yearly basis. Tissue will be obtained at time of biopsy and mastectomy. Should recurrences follow, metastastic tissue would undergo the same testing procedure. During the first year approximately 150-180 patients with primary breast cancer and an additional 50 patients with benign disease will be entered into the study. Twenty to twenty-five specimens of normal breast tissue (from autopsy specimens) will also be assayed. Tissue and serum biochemical-immunochemical data will be compared and changes and differences related to the clinical status of the patient.

Progress: New Contract

Significance for Cancer Research (NCP Objective 5 Approach 5.4)

Project Officer: Bernice T. Radovich, Ph.D.
Program: Breast Cancer Diagnosis Site Visit Date: 4/12/77
Technical Review Group: Breast Cancer Diagnosis Committee
Relevance Review Group: Breast Cancer Task Force Steering Committee
FY 77 Funds: $97,300

CONTRACT RESEARCH SUMMARY

Title: Biologic Markers in Breast Cancer: Patient Resource

Principal Investigator: Dr. Leslie W. Whitney
Name/Address Wilmington Medical Center
Performing Organization: Wilmington, DE

Contract Number: NO1-CB-74137
Starting Date: 9/1/77 Expiration Date: 8/31/78

Goal: The aim of this project is to develop a Breast Cancer Task Force specimen resource, namely for blood from breast cancer patients and controls to be utilized in a search for and verification of new breast cancer markers.

Approach: Thirty milliliters of blood will be collected from breast disease patients who are scheduled to undergo biopsy and/or primary surgery for breast lesions prior to surgery. Another specimen will be collected, when feasible, 5-10 days postoperatively from the same patient. Specimens will be stored at -70°C, then shipped to NCI designated blood bank facility with appropriate clinical data.

Progress: New Contract

Significance for Cancer Research (NCP Objective 5 Approach 5.4)

Project Officer: Ihor J. Masnyk, Ph.D., Bernice T. Radovich, Ph.D.
Program: Breast Cancer Diagnosis
Technical Review Group: Breast Cancer Biologic Markers Group
Relevance Review Group: Breast Cancer Steering Committee
FY 77 Funds: $30,700

CONTRACT RESEARCH SUMMARY

Title: Biologic Markers in Breast Cancer: Patient Resource

Principal Investigator: Dr. Ned D. Rodes
Name/Address Cancer Research Center
Performing Organization: Columbia, MO

Contract Number: NO1-CB-74138
Starting Date: 9/1/77 Expiration Date: 8/31/78

Goal: To serve as a Breast Cancer Task Force specimen resource, i.e, blood from breast cancer patients and controls to be utilized in a search for and verification of new breast cancer markers.

Approach: Thirty milliliters of blood will be collected from all Breast Cancer Detection Demonstration Projects screenees (approximately 600 per month). One 30-ml postoperative specimen will also be collected from post-biopsy cases within the first month. Another specimen will be collected from previous donors at one year anniversary. All blood will be stored at -70°C, then shipped to NCI designated blood bank facility with appropriate clinical data. This project will consist of a two-year collection and three-year follow-up period.

Progress: New Contract

Significance for Cancer Research (NCP Objective 5 Approach 5.4)

Project Officer: Ihor J. Masnyk, Ph.D., Bernice T. Radovich, Ph.D.
Program: Breast Cancer Diagnosis
Technical Review Group: Breast Cancer Biologic Markers Group
Relevance Review Group: Breast Cancer Steering Committee
FY 77 Funds: $62,700

CONTRACT RESEARCH SUMMARY

Title: Biological Markers in Breast Cancer: Patient Resource

Principal Investigator:	Dr. Harold E. Bowman
Name/Address	Butterworth Hospital
Performing Organization:	Grand Rapids, MI

Contract Number: NO1-CB-74213
Starting Date: 9/15/77 Expiration Date: 9/14/78

Goal: To develop a Breast Cancer Task Force specimen resource, namely for blood from breast cancer patients, benign disease patients and controls to be utilized in a search for and verification of new breast cancer markers.

Approach: Thirty milliliters of blood will be collected from breast disease patients who are scheduled to undergo biopsy and/or primary surgery for breast lesions prior to surgery. Another specimen will be collected, when feasible, 5-10 days postoperatively from the same patient. Specimens will be stored at -70°C, then shipped to NCI designated blood bank facility with appropriate clinical data.

Progress: New Contract

Significance for Cancer Research (NCP Objective 5 Approach 5.4)

Project Officer: Ihor J. Masnyk, Ph.D., Bernice T. Radovich, Ph.D.
Program: Breast Cancer Diagnosis
Technical Review Group: Breast Cancer Biologic Markers Group
Relevance Review Group: Breast Cancer Steering Committee
FY 77 Funds: $19,900

CONTRACT RESEARCH SUMMARY

Title: Application of Flow System Methods of Cell Analysis and Sorting to Cancer Screening

Principal Investigator: Name/Address Performing Organization:	Dr. Paul Mullaney ERDA -- Los Alamos Scientific Laboratory Los Alamos, NM

Contract Number: Y01-CB-60311
Starting Date: 4/1/71 Expiration Date: 4/30/78

Goal: Automation of clinical cytology screening and diagnosis.

Approach: The contractor shall (1) collaborate with Battelle Institute to study light scattering and diffraction, (2) evaluate improved methods of data acquisition and analysis applicable to multiparameter flow systems, (3) implement and test a dual laser sorter using an added UV krypton laser and new stains, and (4) evaluate improved computer interface for existing sorter.

Progress: The contractor has obtained a large number of gynecologic specimens for which some dispersal, fixation, and staining techniques have been developed. The acriflavin-feulgen procedure for DNA staining, mithramycin as a rapid DNA stain, propidium iodide and fluorescein isothiocyanate as a simultaneous DNA-protein staining technique, narrow angle light scatter, multi-angle light scatter, time-of-flight, and Coulter volume parameters have been implemented on flow systems. These show high potential as useful parameters in gynecologic cancer screening. The contractor has also made major improvements in the electronic cell sorting technology which will be used to demonstrate the correlation between these parameters and the morphology.
A dual laser sorter has been constructed and will be tested using a number of fluorochromes. Improved computer interface is undergoing analysis. The collaborative work with Grumman Aerospace Corporation has been concluded.

Significance for Cancer Research (NCP Objective 5 Approach 5.3)
The use of a very rapid zero-resolution automated screening system in clinical cytodiagnosis will allow greater availability of these services to a much larger population with improved diagnostic accuracy.

Project Officer: Bill Bunnag, Ph.D.
Program: Cytology Automation Site Visit Date: 1/5/77
Technical Review Group: Cytology Automation Committee
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $360,000

CONTRACT RESEARCH SUMMARY

Title: Slit-Scan Technique as Cancer Prescreening Automated System in Cytology

Principal Investigator: Name/Address Performing Organization:	Dr. Leon L. Wheeless, Jr. University of Rochester Rochester, NY

Contract Number: N01-CB-33862
Starting Date: 3/19/74 Expiration Date: 3/18/78

Goal: Automation of clinical cytologic screening and diagnosis.

Approach: The contractor will evaluate the VIDICON imaging system. The system is interfaced to the slit-scan flow instrument as a means of imaging cells as they pass through the flow chamber. Causes of false alarms will be determined using this system and ways of eliminating them will be attempted.

Progress: A second bench mark study was completed to evaluate a new sample preparation technique. The false alarm rate was reduced considerably. Two images of an individual cell taken from different angles can now be correlated with that particular cell's slit-scan contour. In this manner cells which cause false alarm signals can be imaged and investigations into possible ways to eliminate these false alarms can be conducted.

Significance for Cancer Research (NCP Objective 5 Approach 5.4)
The development of a flow-through screening system for cervical cytology will allow greater accuracy, speed and availability in screening and diagnosis of cancerous and precancerous lesions.

Project Officer: Mary Cassidy
Program: Cytology Automation Site Visit Date: 6/23/75
Technical Review Group: Committee on Cytology Automation
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $368,741

CONTRACT RESEARCH SUMMARY

Title: New Stains and Other Optical Markers Useful for Gynecologic Specimens

Principal Investigator: Name/Address Performing Organization:	Dr. Brian H. Mayall ERDA - Lawrence Livermore Laboratory Livermore, CA

Contract Number: Y01-CB-40300
Starting Date: 6/1/74 Expiration Date: 6/29/77

Goal: Development and preliminary clinical testing of stains useful in differentiating normal from non-normal cytopathological material.

Approach: Utilizing the unique combination of flow-sorting and image-processing expertise, the contractor will evaluate specimen preparation and staining techniques on clinical samples. The ability to evaluate specimens at both zero and medium to high resolution will assure the mutual compatibility of preparative techniques and safeguard the diagnostic value of samples prepared for automated systems.

Progress: Clinical specimens have been collected and used for production of monodisperse cell suspensions. The cells are treated by mechanical means, e.g., syringing and chemicals, and by enzymes and toxins. Cells of various types have been photographed and mapped for quantitative cytochemistry. The approach ensures that specific cell types are analyzed, as the CYDAC is employed to digitize and compile data on these cells. Correlation between data and selected cells can be made since each cell was previously photographed and recorded. Cells in suspension are also quantitatively analyzed by the LLL flow microfluorometer. Data have been obtained pertaining to different fluorescent properties of the various cell types. More samples are being analyzed. Several fluorochromes have been evaluated for their potential usefulness in cell differentiation. These include: Azure A-Feulgen, naphthol yellow S, BMB (4-bromomethyl-7-methoxy-2-oxo-2H-benzpyran), and chromomycin A3. A dual laser flow system has been implemented and will be used to study cytochemical probes for chromatin structure.

Significance for Cancer Research (NCP Objective 5 Approach 5.3)
Development and evaluation of techniques to rapidly screen cell populations for premalignant and malignant cells.

Project Officer: Bill Bunnag, Ph.D.
Program: Cytology Automation Site Visit Date: 5/14/76
Technical Review Group: Committee on Cytology Automation
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $390,486

CONTRACT RESEARCH SUMMARY

Title: Development of Hematoxylin Substitutes for Staining of Tissues and Exfoliated Cells

Principal Investigator: Dr. Ralph D. Lillie
Name/Address Louisiana State University
Performing Organization: Baton Rouge, LA

Contract Number: N01-CB-43912
Starting Date: 1/11/74 Expiration Date: 1/10/79

Goal: Development of hematoxylin substitutes for diagnostic staining of tissues and exfoliative cells.

Approach: (1) Synthesize various classes of mordant dyes or obtain same from either specific manufacturers or from the archives of the Biological Stain Commission. (2) Perform studies on various tissues with combinations of dyes obtained to achieve staining in accordance with criteria satisfactory to the Project Officer and to the Biological Stain Commission's certification criteria. (3) Procure samples of possibly suitable mordant dyes offering blue or black mordant colors which may be suitable to replace hematoxylin in one or more of its histological staining uses. (4) Subject such samples to the usual tests applied by the Biological Stain Commission for the certification of hematoxylin. (5) Apply favorable test results to routine surgical diagnostic material, in Papanicolaou smear diagnosis, and in other staining procedures applicable to the differential diagnosis of various cancers, evaluating results in each case in comparison of previously standard hematoxylin procedures and with the best of the previously proposed substitutes.

Progress: Synthesis and testing are on schedule as outlined above.

Significance for Cancer Research (NCP Objective 5 Approach 5.3)
Stain development is essential to the cytological diagnosis of cancer.

Project Officer: M. F. Stanton, M.D.
Program: Cytology Automation
Technical Review Group: Ad Hoc Committee Laboratory of Pathology
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $48,911

CONTRACT RESEARCH SUMMARY

Title: Markers for Detection of Abnormal Cervical Cells by Optical Methods

Principal Investigator: Dr. B. D. Halpern
Name/Address Polysciences, Inc.
Performing Organization: Warrington, PA

Contract Number: NO1-CB-43943
Starting Date: 6/1/74 Expiration Date: 5/31/77

Goal: Chemical synthesis and preliminary testing of markers for clinical specimens.

Approach: The contractor will produce absorptive and fluorescent dyes to stoichiometrically quantitate macromolecules, enzymatic activity and antigen-antibody systems suggested by basic scientific research to be of potential utility in distinguishing human malignant and premalignant cells from non-neoplastic cells in automated cytopathologic screening instruments.

Progress: The Contractor has produced various sized fluorescent-labeled microspheres with functional groups. The contractor has also collaborated with other contractors in conjugation of microspheres, rare earth chelate synthesis, and purification of several fluorochromes.

Significance for Cancer Research (NCP Objective 5 Approach 5.3)
Chemical synthesis and verification of stoichiometric stains useful for clinical use in screening cytopathology specimens.

Project Officer: Bill Bunnag, Ph.D.
Program: Cytology Automation Site Visit Date: 10/25/74
Technical Review Group: Committee on Cytology Automation
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: Evaluation of Markers for Gynecologic Specimens

Principal Investigator: Name/Address Performing Organization:	Dr. Torbjorn Caspersson Karolinska Institute Stockholm, Sweden

Contract Number: N01-CB-43945
Starting Date: 6/30/74 Expiration Date: 6/29/78

Goal: Automation of clinical cytologic screening and diagnosis, concomitant with improvement in diagnostic accuracy and throughput.

Approach: Dr. Caspersson has pioneered the development of innovative methods of investigative cytology and cytogenetics. Under this contract, he will develop and evaluate prototype machines for automatically measuring cytologic features of clinical gynecologic specimens using high resolution scanning microscopy with absorption ultraviolet-spectrophotometry, interferometry and cytofluorometry, individually and in combination. Quantitative measurements of the various cell types of the female genital tract will yield multiparameter data which can be used as discriminators for these different cell types by automated cytology instruments.

Progress: A two-parameter instrument has been constructed. The instrument consists of computer-controlled servomotor driven scanning microscope, microspectrophotometer and microinterferometer. The scanning microscope is used to examine and select cells and has the capability to recall the previously chosen cells for reexamination and analysis. The integrated instrument permits microspectrophotometric measurements in the UV and/or visible range, followed by microinterferometric measurements on the same cell while the cell remains in the same microscope field of vision. Modification and improvement of the systems including incorporation of image intensifier-camera system have been completed. Data on gynecologic materials are being accumulated and analyzed.

Significance for Cancer Research (NCP Objective 5 Approach 5.3)
Development of very rapid high resolution multiple modality automated scanning microscopes will advance image processing approaches for cytologic screening and diagnosis, and promote better understanding of normal, precancerous and cancerous states.

Project Officer: Bill Bunnag, Ph.D.
Program: Cytology Automation Site Visit Date: 6/26/76
Technical Review Group: Committee on Cytology Automation
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $46,000

CONTRACT RESEARCH SUMMARY

Title: Evaluation of Stains Useful for Gynecologic Specimens

Principal Investigator:	Dr. Seymour West
Name/Address	University of Alabama
Performing Organization:	Birmingham, AL

Contract Number: N01-CB-43960
Starting Date: 6/30/74 Expiration Date: 6/14/77

Goal: Evaluation of the applicability of biophysical instrumental analysis to clinical cytopathologic pre-screening.

Approach: The contractor will apply biophysical techniques to evaluate acridine orange as a molecular probe and fluorescence fading phenomenon.

Progress: Nuclear fluorescence intensity of fixed cells from clinical gynecologic specimens and acridine orange fluorescent fading of nuclear macromolecules are under investigation.

Significance for Cancer Research (NCP Objective 5 Approach 5.3)
Identification of new machine sensible properties suitable for distinguishing neoplastic from non-neoplastic human cells.

Project Officer: Bill Bunnag, Ph.D.
Program: Cytology Automation Site Visit Date: 11/22/74
Technical Review Group: Committee on Cytology Automation
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: New Stains and Other Optical Markers for Clinical Specimens in Suspension

Principal Investigator:	Dr. Robert C. Leif
Name/Address	Papanicolaou Cancer Research Institute
Performing Organization:	Miami, FL

Contract Number: NO1-CB-43962
Starting Date: 6/30/74 Expiration Date: 6/29/77

Goal: Investigation of new markers and techniques of specimen preparation for clinical cytopathologic screening.

Approach: The investigator will extend the technique of centrifugal cytology to produce improved specimens for analytic instrumentation. Techniques for dialysis staining, heavy metal chelating fluorochromes and immunofluorescence will be investigated as preliminary feasibility studies.

Progress: Dialysis staining machines and centrifugal cytology buckets have been constructed and modified. Cell dispersion studies have been concluded; enzymes and chemicals tested appear to produce cervical, vaginal cell morphologic damage. The value of cervical carcinoma antigens is being further assessed for possible use as abnormal cell markers. The synthesis of rare earth chelates has continued.

Significance for Cancer Research (NCP Objective 5 Approach 5.3)
The development of new markers and preparative techniques for clinical specimens will improve the prospects for more rapid automation of clinical cytopathologic prescreening.

Project Officer: Bill Bunnag, Ph.D.
Program: Cytology Automation Site Visit Date: 6/9/76
Technical Review Group: Committee on Cytology Automation
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: Immunologic Markers Applicable to Cytology Automation

Principal Investigator: Name/Address Performing Organization:	Dr. Harold Haines University of Miami School of Medicine Miami, FL

Contract Number: NO1-CB-74096
Starting Date: 5/13/77 Expiration Date: 5/12/79

Goal: Qualitative and/or quantitative antigenic changes in premalignant and malignant cells will allow discrimination from normal cells.

Approach: Contractor shall isolate and purify cervical carcinoma antigen (CCA). Appropriate antisera to CCA will be prepared and cell by cell analysis using indirect immunofluorescent technique and restaining by Pap staining procedure will be done. Exfoliated cells, tissue imprints and tissue sections will be used. Technique for immunofluorescent staining of exfoliated cells in suspension will be developed for use in flow microfluorometric cell sorter.

Progress: New Contract

Significance for Cancer Research (NCP Objective 5 Approach 5.3)
The development of new markers will improve the prospects for more rapid automation of clinical cytopathologic prescreening.

Project Officer: Bill Bunnag, Ph.D.
Program: Cytology Automation
Technical Review Group: Committee on Cytology Automation
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $120,000

CONTRACT RESEARCH SUMMARY

Title: Immunologic Markers Applicable to Cytology Automation

Principal Investigator: Name/Address Performing Organization:	Dr. Laure Aurelian The Johns Hopkins University School of Medicine Baltimore, MD

Contract Number: NO1-CB-74170
Starting Date: 7/18/77 Expiration Date: 7/17/79

Goal: Qualitative and/or quantitative antigenic changes in premalignant and malignant cells will allow discrimination from normal cells.

Approach: The contractor shall isolate HSV antigens: (i) Total viral antigens, (ii) AG-e and (iii) fractions of AG-e, and prepare corresponding purified antisera to test sensitivity and specificity of these antisera to human gynecologic materials. Immunological and biochemical characterization of the antigens will be done.

Progress: New Contract

Significance for Cancer Research (NCP Objective 5 Approach 5.3)
The development of new markers will improve the prospects for more rapid automation of clinical cytopathologic prescreening.

Project Officer: Bill Bunnag, Ph.D.
Program: Cytology Automation Site Visit Date: 2/24/77
Technical Review Group: Committee on Cytology Automation
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $75,000

CONTRACT RESEARCH SUMMARY

Title: Immunologic Markers Applicable to Cytology Automation

Principal Investigator: Name/Address Performing Organization:	Dr. John J. Docherty Pennsylvania State University University Park, PA

Contract Number: NO1-CB-74171
Starting Date: 7/18/77 Expiration Date: 7/17/79

Goal: Qualitative and/or quantitative antigenic changes in premalignant and malignant cells will allow discrimination from normal cells.

Approach: The contractor shall isolate "tumor antigen" extracted from HSV-1 and HSV-2 transformed cells, and prepare corresponding purified antisera for labeling with peroxidase and fluorescein isothiocyanate and testing on gynecologic exfoliated cervical cells and biopsy specimens. Cell by cell analysis will be done to assess the sensitivity and specificity of the assay. Techniques for immunofluorescent staining of exfoliated cells in suspension will be developed for use with flow microfluorometric cell sorter.

Progress: New Contract

Significance for Cancer Research (NCP Objective 5 Approach 5.3)
The development of new markers will improve the prospects for more rapid automation of clinical cytopathologic prescreening.

Project Officer: Bill Bunnag, Ph.D.
Program: Cytology Automation
Technical Review Group: Committee on Cytology Automation
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $105,825

CONTRACT RESEARCH SUMMARY

Title: Image Processing for Development of Automated Cell Recognition System

Principal Investigator: Dr. George L. Wied
Name/Address University of Chicago
Performing Organization: Chicago, IL

Contract Number: N01-CB-33873
Starting Date: 5/31/73 Expiration Date: 4/30/78

Goal: Automation of clinical cytologic screening and diagnosis, focusing on definition of information requirements and criteria for high throughput, high resolution image processing-based decision making.

Approach: The contractor shall evaluate information requirements for characterization and recognition of normal, premalignant and malignant cells from the human female genital tract by means of digital image processing. Robustness of cytologic features and discrimination logic will be assessed as a function of minor variations in staining and fixation procedures.

Progress: Digitized cell images have been compiled. These data are stored on tapes and will be made available to other contractors for further analyses. These cells are from the various cell types encountered in the exfoliated cell specimens from the female genital tract. Image editing system is operational. Sorted cleaned cell images are available for other contractors to analyze with their own algorithms. Further details on scanned cells are being done using 3-color scanner. New computer program has been written to evaluate the new information. The multi-spectral band scanner has enriched the data base for cell image processing. The new color features enhance the classification of metaplasias, dysplasias and malignant cases. Feature extraction for chromatin distribution patterns has been implemented. High-resolution data acquisition module and Cell Detection Module hardware are being implemented.

Significance for Cancer Research (NCP Objective 5 Approach 5.3)
A rapid, high-resolution, multi-spectral digital scanner for clinical gynecologic screening and diagnosis will promote better health care delivery and therapy monitoring for the populations at large and at high risk.

Project Officer: Bill Bunnag, Ph.D.
Program: Cytology Automation Site Visit Date: 6/8/76
Technical Review Group: Committee on Cytology Automation
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $234,539

CONTRACT RESEARCH SUMMARY

Title: Application of Digital Image Processing Techniques to Cytology Automation

Principal Investigator: Name/Address Performing Organization:	Dr. Raymond Wall JPL -- California Institute of Technology Pasadena, CA

Contract Number: Y01-CB-70314
Starting Date: 9/30/77 Expiration Date: 9/29/79

Goal: Development of optimal algorithms for cell classification applicable to automated digital image processing system.

Approach: The contractor shall determine whether or not current state of the art in pattern recognition is adequate to support the development of an economically viable cytological screening instrument based on single cell classification. Specimen preparation protocol will be optimized so as to produce acceptable single cells for digitization. A large number of digitized images will be accumulated in the library for subsequent feature extraction program to produce a feature data base. A series of classification experiments will be run on the feature data base to select the subsets of cell measurements that yield the best overall performance.

Progress: New Contract

Significance for Cancer Research (NCP Objective 5 Approach 5.3)
Single cell classification algorithms are the key to success in any automated digital image processing system applied to cytology automation.

Project Officer: Bill Bunnag, Ph.D.
Program: Cytology Automation Site Visit Date: 5/23/77
Technical Review Group: Cytology Automation Committee
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $199,992

CONTRACT RESEARCH SUMMARY

Title: Application of Digital Image Processing Techniques to Cytology Automation

Principal Investigator: Dr. James W. Bacus
Name/Address Rush-Presbyterian-St. Luke's
Performing Organization: Medical Center
Chicago, IL

Contract Number: N01-CB-74190
Starting Date: 9/30/77 Expiration Date: 9/29/80

Goal: Development of optimal algorithms for cell classification applicable to automated digital image processing system.

Approach: The contractor shall conduct a comprehensive study to determine single cell vs. specimen classification accuracies for image processing algorithms and for cytotechnologist. This will determine how well the machine algorithms are performing. Five experimental tasks will be done: (1) sample acquisition, (2) cell acquisition, (3) observer recognition, (4) cell classification algorithms development, and (5) analysis and evaluation of results.

Progress: New Contract

Significance for Cancer Research (NCP Objective 5 Approach 5.3)
Single cell classification algorithms are the key to success in any automate digital image processing system applied to cytology automation.

Project Officer: Bill Bunnag, Ph.D.
Program: Cytology Automation Site Visit Date: 5/30/77
Technical Review Group: Cytology Automation Committee
Relevance Review Group: Cancer Diagnosis Steering Committee
FY 77 Funds: $237,000

CONTRACT RESEARCH SUMMARY

Title: Isolation and Characterization of Soluble Human Tumor (CEA)-Specific Antigens

Principal Investigator: Name/Address Performing Organization:	Dr. Ralph A. Reisfeld Scripps Clinic and Research Foundation La Jolla, CA

Contract Number: NO1-CB-43277
Starting Date: 1/1/74 Expiration Date: 2/28/77

Goal: The purification of carcinoembryonic antigen (CEA) from tissue extracts and other fluids utilizing nondenaturing conditions, and the evaluation of these procedures as a means of producing highly specific radioimmunoassay (RIA) reagents.

Approach: CEA has been purified from saline extracts of tumor tissue by the use of lectin-affinity chromatography, molecular sieve chromatography, and isoelectric focusing; serum CEA has been isolated through the use of immunoadsorbents.

Progress: Classical purification procedures result in increased heterogeneity of the CEA population, as evaluated by lectin binding and by molecular sieve chromatography, due primarily to the use of lyophilization procedures for the Purpose of concentrating samples. A procedure was developed for the immunization of animals with serum CEA, or with anti-CEA reactive substances derived from the sera of individuals with other malignancies. Unfortunately, the resulting antisera did not exhibit increased specificity, but the failure of immunoadsorbent-bound cross-reacting antigens to stimulate an anti-CEA response did suggest some differences in these antigens. By employing low concentrations of non-ionic detergents in the RIA incubation mixtures, it was shown that antigenic determinants lost during classical (denaturing) purification procedures could "regenerate," providing further evidence that the loss of antigenic activity after perchloric acid treatment and lyophilization is due to alterations in the antigenic structure of the molecule.

Significance to Cancer Research: If the reagents recently produced are shown to result in an assay of enhanced specificity and/or sensitivity, improved prognostic and diagnostic procedures will be developed, and a means of detecting gastrointestinal neoplasia may result.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: Endoglycosidases Capable of Releasing Oligosaccharides from Glycoproteins

Principal Investigator:	Dr. Om Bahl
Name/Address	State University of New York
Performing Organization:	Buffalo, NY

Contract Number: NO1-CB-43989
Starting Date: 5/1/74 Expiration Date: 7/30/77

Goal: Isolation and characterization of endoglycosidases which are capable of degrading the polysaccharide moiety of glycoproteins.

Approach: The general experimental approach involves (1) the screening of various animal, plant, and microbial sources for endoglycosidase activity, and (2) the enrichment of endoglycosidase activity in the culture medium of bacteria grown on specific carbon sources. A correlated aspect of the work is to prepare suitable substrates for endoglycosidases either from the naturally occurring glycoproteins or by chemical synthesis.

Progress: Glycoproteins have assumed a great deal of importance because of their involvement in a number of disease states, particularly alterations in cell surface glycoproteins during malignancy. Availability of the endoenzymes will not only facilitate understanding of the molecular structure of glycoproteins but also help in delineating the specific parts of the structure related to the disease state. Initial efforts were directed toward the preparation of suitable substrates for the enzymes. Two types of substrates were prepared, one ^{3}H-labeled obtained by the controlled periodate oxidation and reduction and second by the reduction of the carboxyl groups of sialic acid in the glycopeptide from α_1-acid glycoprotein. With the help of these substrates several sources have been screened for endoglycosidase activity. Results of these studies have not been very promising. Consequently, attention was focused on the elaboration of the enzymes by the enrichment technique, i.e., isolation of bacteria which can grow on specific carbon sources, such as polysaccharides, galactomannans, chitin, and yeast mannan. Several bacteria have been thus isolated that produce endoglycosidases which are released in the culture media. Work is in progress to isolate and characterize these enzymes.

Significance to Cancer Research: (NCP Objective 5 Approach 4)

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 76 Funds: $45,103 (TQ)

CONTRACT RESEARCH SUMMARY

Title: Tumor-Specific Antigens in Diagnosis and in the Management of Cancer Patients

Principal Investigator: Name/Address Performing Organization:	Dr. T. M. Chu Health Research, Inc. Roswell Park Memorial Institute Buffalo, NY

Contract Number: N01-CB-33858
Starting Date: 6/25/73 Expiration Date: 10/24/77

Goal: (1) Evaluate the prognostic value of the preoperative CEA relating to disease recurrence or progression; (2) compare the prognostic value of CEA to other major prognostic parameters of colorectal cancer, such as Dukes' classification; (3) develop a predictive model which integrates the CEA levels with other major prognostic variables to determine the probability of recurrence or progression; and (4) implement a clinical plan for patients whose risk of recurrence is greatest based upon preoperative and follow-up CEA measurements.

Approach: This will be done by determining a pretreatment CEA and serial postoperative CEA 4 and 14 days after surgery, and as well as 1 and 2 months and every 3 months thereafter. The patient's clinical information is closely observed and recorded for clinicopathological correlation. In addition, several statistical analyses are performed. Finally, a predictive model will be developed and evaluated clinically.

Progress: A long-term follow-up of prognostic values of the CEA has been studied in 74 patients with resectable colorectal cancer for 12-60 months. A total of 19 developed recurrence of disease. The median time to recurrence was 24.1 months, with the first recurrence at 7.1 months. Fourteen patients died, with the first death occurring at 8.6 months (median time, 39.0 months). Plasma CEA was found to be independent of age, sex, cell differentiation, or site of tumor. A discrete data analysis indicated that the preoperative CEA is a significant indicator of disease recurrence. Based upon various contingency table analyses and tests on a linear logistic model, no significant correlation was shown between CEA and Dukes' classification. However, the combination of CEA and Dukes' was more significant (sensitive) as a prognostic parameter than either indicator alone. Patients with Duke C tumor and an elevated preoperative CEA (>2.5 ng/ml) had the worst prognosis.

Significance to Cancer Research: CEA is a laboratory assay which can be used as an aid in the management of certain cancer patients.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $70,586

CONTRACT RESEARCH SUMMARY

Title: Evaluation of Assays for Circulating Tumor-Associated Antigens: CEA

Principal Investigator:	Dr. Theodore Hersh
Name/Address	Emory University
Performing Organization:	Atlanta, GA

Contract Number: N01-CB-43887
Starting Date: 3/15/74 Expiration Date: 3/14/78

Goal: To determine the clinical usefulness of carcinoembryonic antigen (CEA) and other tumor-associated antigens, such as CEA-S, as adjuncts in the differential diagnosis of gastrointestinal cancer.

Approach: Patients with gastrointestinal symptoms had blood drawn for CEA level and other tumor-associated antigens. The clinical work-up was accomplished as is usual in order to arrive at a specific diagnosis. At the end of the year, the patients were clinically re-evaluated.

Progress: Over 1,600 patients have been enrolled. Blood has been sent to the reference laboratories for CEA and CEA-S assays. The patients were reevaluated at a year's anniversary to verify the initial diagnosis. Preliminary results are being obtained from the computerized data base on 1,156 patients enrolled in the study; 79% had an initial diagnosis of a benign condition, 13% had a malignancy, and in 8% no definitive diagnosis was established. There is a significant overlap between the CEA values of patients with initial benign and malignant diagnoses. Values found for CEA-S indicated that 96.8% of cases with benign disease were in the normal range, compared to 81.5% of those with cancer. For CEA, 10 of 872 (1.1%) of cases with benign diagnoses had values above 20 compared with 23 of 129 (17.8%) patients with malignancy.

Significance to Cancer Research: (Preliminary) There is a considerable overlap of normal and elevated CEA values in cases with benign and malignant conditions of the gastrointestinal tract. This lack of specificity does not make the CEA assay a useful adjunct in the differential diagnosis of cancer.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program Site Visit Dates: 2/14/74; 12/2/75
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $8,508

CONTRACT RESEARCH SUMMARY

Title: Evaluation of Assays of Circulating Tumor-Associated Antigens: AFP and HCG

Principal Investigator:	Dr. Melvin Moore
Name/Address	Emory University
Performing Organization:	Atlanta, GA

Contract Number: NO1-CB-43888
Starting Date: 3/15/74 Expiration Date: 3/14/77

Goal: To evaluate the sensitivity and specificity of serum HCG and AFP values in the diagnosis of testicular masses. To correlate levels of HCG and AFP with disease activity in germinal testicular malignancies.

Approach: AFP and HCG values are followed serially in patients with known testicular tumors and correlated with disease activity, as well as prior to diagnosis or orchiectomy.

Progress: Prior to diagnosis, elevated markers were seen in 66% (4/6) of patients with non-seminomatous germinal tumors, 25% (2/8) of patients with seminoma, and 0% of patients (0/29) without germinal tumors. Marker studies were obtained in an additional 52 patients after orchiectomy. No elevations of HCG or AFP were seen in 4 patients with non-germinal tumors. Among patients with clinically active germinal tumors, 0% (0/2) of seminoma patients and 74% (14/19) of non-seminoma patients had elevated HCG or AFP levels. Among germinal tumor patients without clinically active disease 0% (0/8) of seminoma patients, and 11% (2/19) on non-seminoma patients had elevated HCG or AFP levels. In this series of patients there were no false positive preoperative elevations of AFP and HCG in patients with testicular masses. Elevations of AFP or HCG in the absence of clinical disease were seen in 7% (2/27) of patients with prior history of germinal tumors and in 0% (0/34) of patients with no prior history of germinal tumors. Among patients with active germinal malignancy, 28% of those with non-seminomatous tumors had falsely negative normal markers as compared with 80% of those with seminoma. The clinical course closely paralleled fluctuations in HCG or AFP in 20/22 patients with elevated marker levels.

Significance to Cancer Research: The tumor markers HCG and AFP have been shown to be quite specific in the diagnosis of germinal tumors of the testes in the young male patient presenting with a testicular mass. The clinical utility of following HCG and AFP serially in patients with non-seminomatous testicular tumors has also been demonstrated. Marker studies are rarely abnormal in patients with seminoma.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program Site Visit Date: 12/2/76
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: Evaluation of an Isomeric Species of Carcinoembryonic Antigen (CEA-S)

Principal Investigator:	Dr. Robert M. Nakamura
Name/Address	Scripps Clinic and Research Foundation
Performing Organization:	La Jolla, CA

Contract Number: NO1-CB-53934
Starting Date: 5/16/75 Expiration Date: 5/15/78

Goal: CEA-S is a specific isomeric species of carcinoembryonic antigen which is found predominantly in tumor tissues and can be detected in fetal and normal body fluids. The workscope of the contract is (1) to isolate and characterize CEA-S from colon carcinomas; (2) to produce specific antisera to CEA-S; and (3) develop an optimally specific and sensitive and standardized assay system for CEA-S.

Approach: General experimental approach to achieve these objectives is (1) isolation of the CEA-S ligands from several colonic carcinomas; (2) comparison of the ligands against a panel of sera with various diseases including gastrointestinal tumor, normal sera, inflammatory bowel disease, and renal diseases; (3) production of the antisera to CEA-S and conventional CEA; and (4) determination of the contribution of potentially interfering glycoproteins to the CEA-S assay such as normal cross-reacting glycoprotein (NCA).

Progress: (1) CEA-S has been isolated from a total of eight tumors; (2) the ligands have been compared against a panel of 65, including pools of normal gastrointestinal, other neoplasias, and renal inflammatory bowel diseases; (3) ten different antisera have been evaluated in the CEA-S assay and, based on diagnostic specificity, the optimal antiserum has been identified; (4) normal cross-reacting glycoproteins have been isolated and a specific radioimmunoassay developed; (5) for the past year panels of serum have been received from Drs. T. Hersh and Ming Chu (Emory University and Roswell Park, respectively), and these panels have been assayed and have been returned to NCI for evaluation.

Significance to Cancer Research: The serum CEA-S assay will be a more standardized assay which has greater specificity for gastrointestinal tumor than the conventional CEA assay. This CEA-S assay will definitely be more helpful in the evaluation of patients with bowel cancer and aid in the differential diagnosis of bowel cancer versus inflammatory bowel disease.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $121,005

CONTRACT RESEARCH SUMMARY

Title: Diagnostic Applications of Human Tumor-Associated Antigens

Principal Investigator: Dr. Ilkka P. T. Hakkinen
Name/Address Turku University
Performing Organization: Turku, Finland

Contract Number: N01-CB-64070
Starting Date: 6/30/76 Expiration Date: 6/29/78

Goal: The project aims to establish the FSA test in screening for early gastric cancer, including characterisation of the FS-antigen, standardisation of the reaction and testing the method by screening an unselected population for gastric cancer as well as discriminating between benign and malignant gastric ulceration, using a clinical series.

Approach: Acid glycoproteins from gastric juice are tested by immunodiffusion against fetal sulphoglycoprotein antiserum. Preparation of the antiserum will be standardized. Subjects secreting FSA will be submitted to clinical examination (gastroscopy). The entire cohort will be followed for two years and the cancer rates of an extensive series compared with existing statistics.

Progress: More than 95% of gastric cancers secrete FSA in gastric juice. The number of people over 40 who secrete FSA does not exceed 7%. It can be seen that clinical examination of this high-risk group is within the limits of feasibility. Further studies on the structure of FSA and on the development of FSA-RIA are in progress. About 30,000 people have been tested by the FSA method. Clinical findings support the working hypothesis that FSA is a marker of a high-risk group for gastric cancer and that early cancers can be detected by this method. Up to now, 21 out of 24 gastric cancers in the FSA-positive material were operable and without metastasis which gives promise of a better prognosis.

Significance to Cancer Research: If the method can be proved to be practical, it will provide a new tool for the early diagnosis of gastric cancer.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $30,354

CONTRACT RESEARCH SUMMARY

Title: Animal Models for Circulating Tumor-Associated Antigens for Diagnosis of Cancer

Principal Investigator: Dr. James W. Osborne
Name/Address University of Iowa
Performing Organization: Iowa City, IA

Contract Number: NO1-CB-43891
Starting Date: 6/1/74 Expiration Date: 5/31/77

Goal: Perform studies of circulating tumor-associated antigens in animal carcinomas that would serve as a model for common human cancers and that are potentially useful in developing immunodiagnostic tests for cancer.

Approach: Study antigens associated with radiation-induced intestinal tumors in rats. Demonstrate and isolate circulating tumor-associated antigens and quantitate the antigen. Study, if possible, the relationship of antigen appearance to premalignant lesions and determine the levels of antigens in relation to tumor size.

Progress: A tumor-associated protein (TAP) was found in an x-irradiation-induced intestinal adenocarcinoma of the rat. The glycoprotein was associated with the tumor cell membranes and shared common antigenic determinants both with rat fetal protein and perchloric acid-soluble protein isolated from the serum of tumor-bearers. Some tumor-bearing animals had decreased levels of the circulating TAP, but a definite correlation between tumor size and serum levels of TAP has not yet been achieved. The immunological activity of the TAP was acid labile, yet alkali and heat stable. Endo- and exopeptidases eliminated discernible immunological activity, but nucleotidases and neuraminidase did not. Purification of 3M KCl extracts was done. A radioimmunoassay for the purified protein was recently developed, but further purification is needed to increase the specific activity of the radiolabeled derivative so that serum levels may be determined.

Even though the oncofetal protein has not yet been fully characterized, it has been determined that KCl extracts block the cytotoxicity of lymphocytes (from tumor-bearing rats) to cultured cells of the tumor. This indicated that the tumor is immunogenic in the host and that blocking factors are also present.

Significance to Cancer Research: The study of this animal model of intestinal carcinoma is of potential importance for determining whether the level of circulating oncofetal protein will be a useful immunodiagnostic tool for cancer. It is especially significant since the morphological and immunological features of the tumor are quite similar to colon and rectal cancer in man.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: Biochemistry and Diagnostic Use of Human Tumor Antigens

Principal Investigator: Name/Address Performing Organization:	Dr. Vincent Marchesi Yale University School of Medicine New Haven, CT
Contract Number: N01-CB-43859	
Starting Date: 8/8/73	Expiration Date: 11/7/76

Goal: To develop a more discriminating radioimmunoassay for the detection of human carcinoembryonic antigens.

Approach: A new method was developed for the isolation of glycoproteins from human colonic cancer tissue employing detergent extraction and lectin affinity chromatography. Partially purified glycoproteins were chemically cleaved at selective segments of their polypeptide chains, and individual glycopeptides were isolated, purified, and analyzed for their immunological activity.

Progress: Antisera were raised in rabbits to partially purified colonic tumor glycoproteins. Specific antibody populations were isolated by immunoadsorption with purified peptides. Antisera prepared by this approach reacted specifically with extracts from human colonic cancer tissue. Cross reactions were noted with "standard" CEA preparations and the CEA-S prepared by Edgington. A preliminary screening test was carried out with these antisera using human samples provided by NCI. These results suggest that the antisera prepared by this approach may have great specificity for antigenic determinants of human colonic cancer tissue.

Significance to Cancer Research: These results suggest that the development of antibodies to specific antigenic determinants of tumor-associated glycoproteins might be an effective way to produce discriminating antisera which can be used to measure the presence of tumor-associated antigens in human serum.

Project Officer: J. Frederic Mushinski, M.D.
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: Development of Immunodiagnostic Tests for Cancer

Principal Investigator:	Dr. Ronald Stevens
Name/Address	University of California
Performing Organization:	Los Angeles, CA

Contract Number: N01-CB-43860
Starting Date: 9/1/73 Expiration Date: 12/31/76

Goal: To identify new tumor-associated antigens in carcinomas of the colon, stomach, lung, breast, prostate, and bladder which might be useful for immunodiagnosis.

Approach: Extract antigens from these carcinomas and from comparable normal tissues and from fetal tissues and prepare heterologous antisera against each of the antigens. Antigens shall be purified and antisera rendered specific for tumor-associated antigens. Radioimmunoassays shall be developed for the detection of each antigen in serum or urine.

Progress: Four antigens have been detected and may represent lung tumor-associated antigen. An antigen(s) NL-1 has been identified and is characteristic of normal lung and of some adenocarcinomas of the lung. Another antigen of M.W. 35,000 has been detected and seems to be confined to and produced by lung tumor cells. Two other antigens were found to be present in extracts of lung tumor tissue and absent in extracts of normal lung tissues. Preliminary radioimmune assays have been developed.

Significance to Cancer Research: New and more specific immunodiagnostic tests for the common types of human cancer are needed.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program Site Visit Date: 7/23/75
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: Human Tumor-Associated Antigens of the GI Tract Other Than CEA and α-Fetoprotein

Principal Investigator:	Dr. Elliot Alpert
Name/Address	Massachusetts General Hospital
Performing Organization:	Boston, MA

Contract Number: NO1-CB-43889
Starting Date: 6/1/74 Expiration Date: 5/31/77

Goal: The goal of this contract has been to search for new human tumor-associated antigens of the gastrointestinal tract other than carcinoembryonic antigen and alpha-fetoprotein.

Approach: The approach has been to render rabbits tolerant to normal plasma and tissue extracts and to immunize with cytoplasmic and membrane extracts as well as with intact tumor cells, in an attempt to raise heterologous antisera to tumor-specific antigens.

Progress: A total of 54 cancer tissues, from malignancies of the stomach, pancreas, colon and liver, were extracted in either saline or 3M KCl or were dissociated into isolated cell preparations. A total of 63 normal tissues were also collected and extracted or prepared as controls. Partial immune tolerance to normal human serum, plasma, and normal tissue antigens was induced in 71 rabbits. These rabbits were then immunized with cancer extracts or isolated cell preparations prepared from fresh human primary liver carcinoma and colon carcinoma tissue or cancer cell lines of human origin. Pools or antisera from the 50 rabbits have been completely absorbed to pools of normal human plasma, serum, and normal tissue extract antigens and tested against cancer tissue, membrane, or cell extracts. Cancer extract antigens absorbed were eluted and appeared as two distinct bands on polyacrylamide gel electrophoresis. Five antisera pools still contained precipitins to either KCl or PBS extracts of tumor tissue and appear to recognize tumor-specific antigens in two malignancies.

Significance to Cancer Research: There is increasing evidence that malignancies of the gastrointestinal tract contain tumor-specific antigens other than CEA and AFP. Our recent data suggest that heterologous antisera can be raised to these antigens. If specificity of these antisera to human tumor-specific antigens can be confirmed by further testing, it would enable isolation and characterization of these antigens, as well as the development of a new immunodiagnostic test for GI malignancy.

Project Officer: R. Raymond Gantt, M.D.
Program: Tumor Immunology Program Site Visit Date: 4/5/74
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: Human Tumor-Associated Antigens of the GI Tract Other Than CEA and Alpha-Fetoprotein

Principal Investigator:	Dr. Peter H. Schur
Name/Address	Robert B. Brigham Hospital
Performing Organization:	Boston, MA

Contract Number: N01-CB-43958
Starting Date: 6/1/74 Expiration Date: 5/31/77

Goal: The goal of this contract has been to search for new human tumor-associated antigens of the gastrointestinal tract other than carcinoembryonic antigen and alpha-fetoprotein.

Approach: The approach has been to render rabbits tolerant to normal plasma and tissue extracts and to immunize with cytoplasmic and membrane extracts as well as with intact tumor cells, in an attempt to raise heterologous antisera to tumor-specific antigens.

Progress: A total of 54 cancer tissues, from malignancies of the stomach, pancreas, colon and liver, were extracted in either saline or 3M KCl or were dissociated into isolated cell preparations. A total of 63 normal tissues were also collected and extracted or prepared as controls. Partial immune tolerance to normal human serum, plasma, and normal tissue antigens was induced in 71 rabbits. These rabbits were then immunized with cancer extracts or isolated cell preparations prepared from fresh human primary liver carcinoma and colon carcinoma tissue or cancer cell lines of human origin. Pools of antisera from the 50 rabbits have been completely absorbed to pools of normal human plasma, serum, and normal tissue extract antigens and tested against cancer tissue, membrane, or cell extracts. Cancer extract antigens absorbed were eluted and appeared as two distinct bands on polyacrylamide gel electrophoresis. Five antisera pools still contained precipitins to either KCl or PBS extracts of tumor tissue and appear to recognize tumor-specific antigens in two malignancies.

Significance to Cancer Research: There is increasing evidence that malignancies of the gastrointestinal tract contain tumor-specific antigens other than CEA and AFP. Our recent data suggest that heterologous antisera can be raised to these antigens. If specificity of these antisera to human tumor-specific antigens can be confirmed by further testing, it would enable isolation and characterization of these antigens, as well as the development of a new immunodiagnostic test for GI malignancy.

Project Officer: R. Raymond Gantt, M.D.
Program: Tumor Immunology Program Site Visit Date: 4/5/74
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: Search for New Human Tumor-Associated Antigens in Carcinoma of the Lung

Principal Investigator: Dr. Robert W. Veltri
Name/Address West Virginia University
Performing Organization: Morgantown, WV

Contract Number: N01-CB-43890
Starting Date: 5/16/74 Expiration Date: 5/15/78

Goal: Search for new tumor-associated antigens in carcinoma of the lung, which may be more useful in immunodiagnosis than currently available markers.

Approach: Lung tumor tissue, normal lungs, and embryonic lungs are processed by a variety of chemical, physical, and mechanical procedures. Antisera to these soluble and membrane extracts are raised in rabbits and absorbed until reactive only with tumor extracts. The antigens thus identified are further characterized and purified for the development of sensitive serum screening procedures.

Progress: With the above approach three proteins have been identified in soluble extracts of human lung carcinomas. These have been called LTAA-1, 2,3. LTAA-1 has been identified as a serum protein present in Cohn fraction IV-4 of human serum and present in lung tumors in large excess. LTAA-2 has been identified as a ferritin and LTAA-3 has been shown to react with commercial antiserum to human lactoferrin. These three antigens have been purified, large volumes of monospecific antiserum prepared, and RIAs are being developed to screen for one or more of them in sera of patients with lung cancer, benign lung disease, and in normal controls. Two other proteins, LTAA-4,5, have been identified in Triton X-100 extracts of lung tumor membranes. As was the case for soluble LTAA-1,2,3 the membrane-associated LTAA-4 and 5 are not CEA, AFP or β_2-microglobulin. LTAA-4 and 5 have been separated by ion exchange chromatography and monospecific antisera are being raised to these antigens. Again the antisera will be used in the development of diagnostic immunoassays. Major emphasis is being directed toward development of RIAs for lung TAAs 3, 4 and 5.

Significance to Cancer Research: (NCP Objective 5 Approach 4)

Project Officer: J. Frederic Mushinski, M.D.
Program: Tumor Immunology Program Site Visit Date: 3/15/74
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $71,400

CONTRACT RESEARCH SUMMARY

Title: Antibodies to Human Organ- or Tissue-Associated Antigens

Principal Investigator: Dr. Jen-Fu Chiu
Name/Address Vanderbilt University
Performing Organization: Nashville, TN

Contract Number: NO1-CB-53896
Starting Date: 6/16/75 Expiration Date: 6/15/78

Goal: To detect antibodies to human organ- or tissue-associated antigens to use in study of antigenic profile of normal and neoplastic cells, both from biopsy and tissue culture.

Approach: Obtain specific antibodies to chromosomal nonhistone proteins associated with homologous DNA, and measure in tumor cells the quantitative decrease or loss of normal antigens and increase of tumor-specific antigens. Distribution and expression of these antigens will be studied in relation to disease type, stage of disease, and prognosis.

Progress: Tissue-specific antisera were obtained against human lung carcinoma, breast carcinoma, and HeLa S_3 cell dehistonized chromatin. The specificity of these antisera was determined by complement fixation. Only chromatins from specific tissues or cells fixed the complement significantly, while chromatins isolated from other human tumors were negative. Localization specificity of antisera against human lung carcinoma was studied with lung carcinoma and normal lung adjacent to tumor. The localization studies indicated that there is no tumor-specific antigen present in normal lung. Studies on the immunospecificity of chromatins isolated from G_1, S, and G_2 phases of HeLa S_3 cell cycle showed that chromatin isolated from G_2 showed much higher immunoactivity than chromatin isolated from other phases. Human lung carcinoma chromatin was fractionated to study the immunoactivity of its components. DNA, RNA, and histones were not responsible for the observed immunospecificity. Two subfractions of nonhistone proteins represented most of chromosomal nonhistone proteins.

Significance to Cancer Research: Developing specific and sensitive antibodies against human organ- or tissue-associated antigens, including tumors, for immunodiagnosis, has a high priority.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program Site Visit Date: 4/25/75
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $95,406

CONTRACT RESEARCH SUMMARY

Title: Diagnostic Application of Human Tumor-Associated Antigens

Principal Investigator:	Dr. Kenneth O. Lloyd
Name/Address	Sloan-Kettering Institute for Cancer Research
Performing Organization:	New York, NY

Contract Number: N01-CB-64021
Starting Date: 6/30/76 Expiration Date: 6/29/78

Goal: The aim of this project is to purify human ovarian cancer antigens which can be detected using heterologous antisera and to develop sensitive assays for these antigens. These assay systems will then be used to detect the antigens in sera of women with ovarian cancers and of suitable controls to determine their usefulness in the diagnosis of ovarian cancer.

Approach: The approach entails the use of heteroimmune sera to detect and assay tumor-associated antigens in ovarian tumors and sera from cancer patients.

Progress: The antigenicity of ovarian tumors is well documented in the literature; numerous antigenic reactions have been described but the corresponding antigens have not been well characterized. Five ovarian tumor-associated antigens were identified using heteroimmune sera. Two of these appear to be new ovarian antigens with potential usefulness in immunodiagnosis. The others are previously described antigens: pregnancy-zone protein (PZP), carcinoembryonic antigen (CEA), and normal glycoprotein (NGP). Purification of the two new antigens (OvC-1 and OvC-2) is in progress. OvC-1 and OvC-2 have molecular weights of about 60,000 and 45,000, respectively. OvC-2 is confined to ovarian tumors, whereas OvC-1 has a somewhat more widespread distribution, being also found in some other tumors and in small amounts in some normal tissues (lung and kidney). Once the antigens have been purified, they will be used to raise more specific antisera and an assay system will be developed for their detection in sera of cancer patients and controls.

Significance to Cancer Research: Ovarian cancer has a high death rate because diagnosis and surgical removal are often critically delayed due to its deep location and lack of early symptoms. Immunodiagnostic assays are aimed at the early detection of ovarian tumors in asymptomatic women.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $72,973

CONTRACT RESEARCH SUMMARY

Title: Diagnostic Applications of Human Tumor-Associated Antigens

Principal Investigator: Name/Address Performing Organization:	Dr. E. Russell Alexander University of Washington Seattle, WA

Contract Number: N01-CB-64068
Starting Date: 6/1/76 Expiration Date: 5/31/78

Goal: To develop and purify an antigen and antiserum which are associated with epidermoid carcinoma of the cervix. To develop methods to use that antigen and antiserum in serological studies.

Approach: Monospecific rabbit antiserum is being prepared against the tumor-associated antigen. Affinity chromatography is being used for purification of antigen based on monospecific antiserum, which purified antigen and monospecific antiserum will be used to detect circulating antibody and antigen by different serologic techniques.

Progress: Work has progressed in the development of a pure monospecific antiserum. When this serum reacts against crude tumor antigen in two-dimensional immunoelectrophoresis, a single precipitin line results. This antigen has been demonstrated by two-dimensional immunoelectrophoresis in 19 cervical cancer tissues, but was absent in 10 other gynecologic cancers and 9 normal gynecologic tissues (including 7 specimens of normal cervical tissue). The antigen is a protein with a molecular weight of approximately 74,000 daltons. When 7 cervical cancer specimens were examined by immunofluorescent antibody methods using "monospecific" antiserum, antigen was seen in both membrane and cytoplasm of cervical cancer cells and was absent in 5 specimens from other gynecologic tumors and 4 normal cervical and 2 normal ovarian preparations. By rocket electrophoresis, the antibody did not detect circulating antigen in serum of cancer patients. However, this antibody did detect circulatory antigen by Ouchterlony immunodiffusion in 2/30 cancer patients' sera and 0/30 control sera.

Significance to Cancer Research: The basis of this study is to develop an immunodiagnostic method for early detection of cervical cancer, and to determine the relationship of such a detection to the development of abnormal cervical cytology (Papanicolaou smear). Of particular concern will be study of the origin and character of this antigen and any possible relationship to the cause of cervical cancer.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $108,032

CONTRACT RESEARCH SUMMARY

Title: Diagnostic Application of Human Tumor-Associated Antigen

Principal Investigator: Dr. Robert Humphreys
Name/Address University of Massachusetts Medical School
Performing Organization: Worcester, MA

Contract Number: NO1-CB-64072
Starting Date: 6/30/76 Expiration Date: 6/29/78

Goal: The objective of this study is to identify and isolate membrane proteins from leukemic cells in order to raise rabbit antibodies which may be used to diagnose biologic subsets of leukemias and lymphomas by cytotoxic or immunofluorescent assays.

Approach: In order to identify subsets of leukemias, membrane proteins from leukemic cell lines are examined by $[^{35}S]$methionine, autoradiographic techniques in SDS polyacrylamide slab gel electrophoresis. T- and B-specific proteins are identified. These proteins are then isolated by traditional protein chemical techniques. Antisera to these proteins are assayed for their specificity for leukemia or for subsets of leukemias.

Progress: Prior to this contract, the investigator found and isolated p23,30, a B lymphocyte-specific marker which identified a biological subset of patients with acute lymphoblastic leukemia. In the first year of this contract the focus has been on comparing SDS polyacrylamide membrane patterns of T and B lymphocytic leukemia cells. B cell patterns are similar to each other while two cell lines, HSB and CEM, differ from each other and from B-cell patterns. Putative B- and T-specific membrane proteins have been identified in these analytic gels. Several proteins have been isolated from membranes by traditional techniques. One of these proteins, p46 from the CEM line, appears to be specific for a subpopulation of normal peripheral blood T lymphocytes. Antisera to other proteins are cytotoxic for lymphocytes and are being characterized. A B-cell antigen of 92,000 daltons has been found. In the coming year these antigens will be characterized in detail and the use of antisera to them for leukemia diagnosis will be tested.

Significance to Cancer Research: The identification of biological subsets of leukemias, as in the case of p23,30-positive ALL patients, permits correlation to the clinical course. These assays may in time affect the selection of chemotherapeutic protocols based on the identification of biological subsets of cancers, or the antisera may be used to modify the immune response in patients with cancer.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $83,130

CONTRACT RESEARCH SUMMARY

Title: Early Detection of Antibodies to Carcinomas in Experimental Animal Models

Principal Investigator: Dr. Lionel Manson
Name/Address Wistar Institute
Performing Organization: Philadelphia, PA

Contract Number: NO1-CB-43882
Starting Date: 6/1/74 Expiration Date: 5/31/77

Goal: Development of experimental animal systems for the early detection of antibody response to tumor-associated antigens, as model for problem of antibody detection in patients with carcinomas and other malignant diseases.

Approach: Studies will be performed with primary, autochthonous carcinomas or with carcinomas in early transplant, in inbred strains of mice. A sensitive antiglobulin assay will be used to determine antibody levels.

Progress: The previously used assay in this study, in which adherent live cells were used as the solid phase immunoadsorbent, was found to be unsuitable for a quantitative antibody assay. By binding membrane, antigenic fragments to activated filter paper discs, a solid phase immunoadsorbent was developed with which absolute quantitation was achieved. By using these discs and specific antibody in an inhibition mode antigen can also be measured. Further studies with the spontaneous mammary adenocarcinoma A-10 have confirmed the previous observations that the cell line appears not to be immunogenic in the A/J mouse. Control experiments with an allogeneic tumor have shown that if antibody appeared in the serum during the early growth of the tumor, it should have been detected by the assay used.

Significance to Cancer Research: (NCP Objective 5 Approach 1)

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program Site Visit Date: 2/27/76
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: Immunofluorescent Detection of Antibodies Against Autologous Human Tumor Cells

Principal Investigator: Name/Address Performing Organization:	Dr. George J. Friou University of Southern California Los Angeles, CA

Contract Number: NO1-CB-43881
Starting Date: 6/1/74 Expiration Date: 5/31/77

Goal: Study of sera of patients with breast carcinoma for presence of antibodies to autologous tumor cells using immunofluorescence, studying surface and intracellular antigens, immunoglobulin class and specificity of observed reactions, and relationship of antibodies to stage and course of disease, screening tests for cell-mediated immunity, and presence of autoantibodies.

Approach: Primary site specimens were obtained from untreated patients. Preoperative, postoperative, and follow-up sera, clinical, pathological data collected. Preoperative sera were tested against autologous viable tumor cells and fixed cell smears, and selected follow-up sera similarly tested. Ig class of antibodies in selected sera was determined. Allogeneic tests and absorptions have been used to evaluate specificity of observed reactions.

Progress: Initial studies included lung and colon as well as breast, but later work was restricted to breast carcinoma patients. Studies prior to the present contract year established that antibodies to autologous surface and intracellular antigens were present in 16/41 (39%) and 29/52 (55%) of breast cancer sera, respectively. Allogeneic tests with cancer sera showed consistency of reactions; controls showed no surface reactions, and 12-13% intracellular reactions. Sera of patients with biopsy-confirmed fibrocystic disease and fibroadenoma showed reaction frequencies with intracellular antigens similar to sera of cancer patients.

Current year studies have included absorptions showing shared antigens between ductal carcinoma and fibroadenoma. Stage 4 sera fail to react in autologous reaction, but cross-testing of stage 1, 2 and 4 sera indicates this to result from antigenic change in stage 4 cells rather than absence of antibody in stage 4 sera. Other clinical correlations, autoantibody studies, and relationship to embryonic antigens are in completion phase.

Significance to Cancer Research: Antibodies detected may assist in cancer diagnosis, or in screening for premalignant lesions. Failure of reactions of positive sera with stage 4 cells has important conceptual relevance to understanding of mechanisms of tumor progression.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer of Immunodiagnosis
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: Detection of Antibodies Against Autologous Human Tumor Cells

Principal Investigator: Name/Address Performing Organization:	Dr. Fiorenzo Paronetto Mt. Sinai School of Medicine New York, NY

Contract Number: N01-CB-43953
Starting Date: 5/16/74 Expiration Date: 5/15/77

Goal: Determine the feasibility of cancer diagnosis through the presence of antibodies against autologous tumors utilizing fluorescent antibody techniques.

Approach: Tumor tissues and sera from patients with tumors of colon and breast were tested for the presence of autoantibodies using the fluorescent antibody technique.

Progress: Utilizing fluorescent antibody techniques, the contractor has previously demonstrated in vitro complement fixation in 68% (21/31) of carcinomas of the colon. IgG autoantibodies against tumors were seen in only 4.5% (1/22) of sera of patients with carcinoma of the colon and 6.5% (2/31) of sera of patients with carcinoma of the breast. Utilizing cell suspension techniques, IgG autoantibodies were detected in sera of 20% (2/10) of patients with carcinoma of the colon. Fifty percent (2/4) of sera of normal controls likewise contained IgG antibodies against the carcinoma cell suspensions which were positive with autologous sera. Sixteen percent (3/19) of sera of patients with colon carcinoma and 16.5% (2/12) of sera of normal controls contained homologous antibodies against an established colon tumor line (HT-29). IgG antibodies active at 4°C (cold antibodies) against autologous carcinoma were detected in 83% (5/6) of sera of patients with carcinoma of the breast. Similar cold antibodies against homologous carcinoma of the breast were detected in 49% (18/37) of normal sera and 60% (22/37) of sera of patients with carcinoma of the breast. Strong cold antinuclear antibodies were detected in 44% (12/27) of sera of patients with carcinoma of the breast, but only in 11% (3/27) of sera of normal controls.

Significance to Cancer Research: The presence of antibodies against tumor in a large proportion of normal sera precludes the use of these antibodies for tumor diagnosis. The antibodies may, however, play a significant role in natural immunity against tumors.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program Site Visit Date: 2/3/76
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: Blood Sample Collection Bank as Reservoir for Evaluation of Cancer Detection Tests

Principal Investigator:	Dr. Allan Schutt
Name/Address	Mayo Foundation
Performing Organization:	Rochester, MN

Contract Number: NO1-CB-23879a
Starting Date: 6/15/72   Expiration Date: 11/14/77

Goal: To establish and maintain a bank of sera from patients with cancer, with benign diseases and from normal individuals.

Approach: Make necessary serum samples available for evaluation of immunodiagnostic tests for cancer. Serve as a central facility for storage of serum and plasma specimens collected by other contractors in the Tumor Immunology-Immunodiagnosis Program.

Progress: The Mayo Serum Bank is a central storage area for a large number of blood samples, including those collected by Immunodiagnosis contractors at the Philadelphia Geriatric and the University of Minnesota cancer screening facilities aside from collection of samples. The Mayo Bank also ships panels of serum samples to investigators under the Immunodiagnosis Program's direction to evaluate potential immunodiagnostic tests for cancer in a blind fashion. Over 70 such test panels have been sent out in recent months. Extensive data are kept on all samples and continuous efforts are made to increase deficient areas of benign or malignant diseases.

Significance for Cancer Research: (NCP Objective 5 Approach 4)
This serum bank will provide sera, in sufficiently large quantities and with adequate controls, to efficiently and rapidly evaluate potential immunodiagnostic tests for cancer.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program   Site Visit Date: 2/19/74
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $100,458

CONTRACT RESEARCH SUMMARY

Title: Collection of Sera from Populations with High Cancer Risk

Principal Investigator:	Dr. Henry Altschuler
Name/Address	Philadelphia Geriatric Center
Performing Organization:	Philadelphia, PA

Contract Number: NO1-CB-33914
Starting Date: 6/25/73 Expiration Date: 10/24/77

Goal: To collect serial serum specimens from populations at high risk of contracting malignant disease for the purpose of developing and evaluating immunodiagnostic screening tests for human cancer.

Approach: Demographically stable populations at high risk of developing human malignancies in the colon, lung, breast, prostate, bladder, pancreas, etc. will be followed on an annual basis. This includes clinical evaluation and serum collection. The sera will be banked and records kept on the patients so that information obtained from the stored sera can be correlated with development of any particular cancer.

Progress: Sera are being continually collected from a demographically stable population of high cancer risk aged residents of the Philadelphia Geriatric Center as well as from others. Complete records are being kept on each patient, including medical information and follow-up data from such sources as autopsies and Tumor Board Conferences. The collected sera are being sent to Mayo Clinic for storage under Dr. Schutt's project. As of February 28, 1977, a total of 2,816 serum samples were collected and 2,759 such samples were shipped. During this period there has been a total of 251 deaths, of which 41 were autopsied. In this same period 40 subjects have developed malignancies. Of these, 23% have G.I. cancers. In the order of decreasing frequencies are cancers of skin, breast, and prostate. In addition, there are a small number of miscellaneous malignancies. It should be pointed out that the population under survey is predominantly female.

Significance to Cancer Research: Early detection of cancer by means of appropriate testing would permit treatment of cancer at the most favorable time.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $52,768

CONTRACT RESEARCH SUMMARY

Title: Collection of Sera from Populations with High Cancer Risk

Principal Investigator:	Dr. John S. Najarian
Name/Address	University of Minnesota
Performing Organization:	Minneapolis, MN

Contract Number: N01-CB-33915
Starting Date: 6/30/73 Expiration Date: 4/30/78

Goal: Serum is collected from individuals in the high cancer risk age group (50 to 70 years of age) during their annual visit to a cancer detection center. The serum is coded, frozen, and stored for future evaluation of potentially promising immunodiagnostic tests for cancer.

Approach: In addition to collection of the serum samples, detailed history is kept which includes the date cancer is detected, and the date and cause of deaths of any members in the study. When the study and collection are completed, this information will be used to designate at least three groups of serum samples: those who never develop cancer; those who develop cancer within a year of the sample; and those developing cancer before the sample is taken. When a new immunodiagnostic test of promise is developed, its potential in early detection of cancer can be validated very quickly by means of this serum bank.

Progress: Since the study started, a total of 5,219 asymptomatic adults have been examined and serum collected for the study. Follow-up on this group indicates that 2,018 have returned for the second visit, and 1,001 for the third visit. Total exams on this population performed have been 8,565. To date, there have been 35 deaths in the population and a total of 94 malignancies, 57 of these were detected at the time of the examination, and 37 developed between visits. Documentation of the malignancy includes the type of tumor, its location, date detected, date confirmed, and the type of treatment the patient received.

Significance to Cancer Research: The importance of early diagnosis of cancer has been repeatedly demonstrated and can result in increasing the life span of those involved. The collection of a bank of serum from individuals whose cancer histories have been carefully and accurately documented can reduce the time required to evaluate the potential of a new diagnostic test from many years to a few days. This results in tremendous savings of money and, more importantly, reduces the time required for initial determinations of value and establishments of efficacy.

Project Officer: Mrs. Judith M. Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $80,096

CONTRACT RESEARCH SUMMARY

Title: Detection of Circulating Antigen-Antibody Complexes in Cancer

Principal Investigator: Name/Address Performing Organization:	Dr. Ralph E. Schrohenloher University of Alabama Birmingham, AL
Contract Number: NO1-CB-53893	
Starting Date: 5/1/75	Expiration Date: 4/30/78

Goal: Establish the presence of circulating immune complexes in cancer and determine the identity, levels, and diagnostic or prognostic value of these materials.

Approach: Develop sensitive and quantitative methods for soluble immune complexes where the antigen is not known, systematically screen sera from a broad cross-section of cancer patients to establish the existence of circulating immune complexes, and establish the identity of the complexes by physicochemical and immunochemical techniques.

Progress: A radioassay based on reaction with human monoclonal rheumatoid factor has been developed. Its capacity to detect circulating immune complexes containing IgG was established using sera and other body fluids from patients with connective tissue diseases associated with a high incidence of these materials. Characterization of the detected materials indicated that the assay is capable of revealing small complexes sedimenting intermediate to 7S and 19S in addition to larger complexes sedimenting at 19S and faster. A radioassay for immune complexes based on inhibition of the binding of radiolabeled Clq to latex-aggregated IgG particles was also developed. The method is rapid, sensitive and semi-quantitative, but lacks the specificity necessary for detection of immune complexes in cancer sera. For this reason a modified assay using Clq is under development. Application of the monoclonal rheumatoid factor assay to screening sera from cancer patients has been initiated.

Significance to Cancer Research: Studies on the occurrence of immune complexes in cancer are of potential significance in understanding the immunobiology of the disease. Procedures for immune complexes also show promise as aides in monitoring disease activity.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $92,741

CONTRACT RESEARCH SUMMARY

Title: Detection of Circulating Antigen-Antibody Complexes in Cancer

Principal Investigator: Name/Address Performing Organization:	Dr. Dieter Burger Washington State University Pullman, WA

Contract Number: N01-CB-63990
Starting Date: 9/1/75 Expiration Date: 8/31/78

Goal: To isolate immune complexes from the circulation and identify the role which these antigen-antibody complexes may play during enhancement or regression of tumor growth.

Approach: Affinity chromatography with immobilized equine complement Clq is used as a sorbent for isolation of complement Clq-fixing immune complexes using feline leukemia as a model for human cancer. Purified immune complexes are quantitated and then identified. These data will be correlated with the clinical status of the animal, presence of leukemia group-specific antigen (gs-antigen), and the titer or antitumor antibody.

Progress: During the present contract year circulating immune complexes were isolated frequently from cats without exposure to feline leukemia virus. A detailed analysis by virus neutralization and fluorescent antibody tests demonstrated that the antibody specificity of these complexes was directed against feline caliciviruses, the causative agents of a common feline respiratory infection. During a chronologic study of circulating immune complexes in two calicivirus-infected kittens, it was observed that the virus infection persisted in the respiratory tract during the entire observation period, whereas the complexemia was temporary (3 weeks) and declined to negative values during the observation period of five weeks. Immune complexes isolated from eight cats which carried protective anti-leukemia (FOCMA) antibody had higher IgG concentration (X 208 μg/ml) than four sera from leukemic, FOCMA negative cats (94 μg/ml). In one cat with a rapidly progressing tumor no complement-fixing immune complexes were found.

Significance to Cancer Research: Our affinity chromatography technique can be used to isolate circulating immune complexes from kryptic disease processes such as cancer, and it may aid in identifying the causes of enhancement of tumor growth.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $57,638 (estimate)

CONTRACT RESEARCH SUMMARY

Title: Detection of Circulating Antigen-Antibody Complexes in Cancer

Principal Investigator: Name/Address Performing Organization:	Dr. Argyrios N. Theofilopoulos Scripps Clinic and Research Foundation La Jolla, CA

Contract Number: N01-CB-53952
Starting Date: 5/16/75 Expiration Date: 5/15/78

Goal: Detection and quantitation of immune complexes (ICs) in sera of patients with malignancies; determining prognostic significance of ICs in monitoring these patients; identification and possible isolation of the tumor antigens in ICs; and production of antisera against tumor antigens in ICs.

Approach: Levels of ICs will be determined by the Raji cell radioimmunoassay. ICs will be isolated using Raji cells or insolubilized conglutinin as substrates. Isolated antigens or ICs will be used for the production of antisera in experimental animals.

Progress: A sensitive and simple procedure for the detection and quantitation of soluble complement-fixing IC in human sera has been developed by utilizing complement receptors on Raji cells. Over 500 patients with various malignancies were studied using this assay. Abnormal levels of ICs were found in from 16 to 52% of patients with different types of tumors. The highest incidence of elevated IC was found in colon carcinoma, melanoma, osteogenic sarcoma, breast carcinoma, and carcinoma of the stomach. The incidence of positivity and the amount of IC found increased with increasing tumor size and with metastatic spread. Immunofluorescence and isotope-labeled antibody techniques showed that IC from sera of patients with melanoma, osteosarcoma, and colon carcinoma which bound to the complement receptors on Raji cells contained respective tumor cell antigens. Techniques were developed for concentrating and isolating preformed IC from human serum as well as sera of experimental animals with serum sickness and transplantable tumors by binding to Raji cells or to insolubilized bovine conglutinin.

Significance to Cancer Research: Tumor antigen-antibody complexes have been implicated as modulators of tumor immunity. Development of techniques for their identification and quantitation may help in monitoring the course of the disease and the effect of treatment in these patients. Isolation of tumor antigens and production of antisera against them will be of extreme importance in understanding the pathogenesis of malignancies and in developing specific diagnostic procedures.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $85,569

CONTRACT RESEARCH SUMMARY

Title: New *In Vitro* Techniques to Evaluate Cell-Mediated Immunity to Intact Tumor Cells

Principal Investigator:	Dr. Christopher S. Henney
Name/Address	Johns Hopkins University
Performing Organization:	Baltimore, MD

Contract Number: N01-CB-43965
Starting Date: 5/16/74 Expiration Date: 5/15/77

Goal: This contract has sought ways in which cell-mediated cytotoxic assays could be adapted to enable detection of cell-mediated immunity against syngeneic tumor.

Approach: Low molecular weight markers have been used to detect minimal membrane permeability changes induced in target cells by lymphocytes. It was hypothesized that by measuring such minimal damage one might be able to increase the sensitivity of cytotoxic assays *in vitro*. Attempts have been made to increase the lytic activity of lymphocytes by culturing effector cell populations under varying conditions before assay.

Progress: Although it could readily be shown that ^{86}Rb flux preceded ^{51}Cr release in cell-mediated lytic assays, we found no evidence that use of the low molecular weight marker increased the sensitivity of the assay. Lesions that initially allow ^{86}Rb efflux do not anneal, but enlarge (probably by colloid osmotic pressures) and eventually allow ^{51}Cr release and disruption of the cell membrane. Culturing mouse effector lymphocytes *in vitro* even for fairly brief (16 hours) periods led to a marked increase in lytic activity. Considerable evidence was gathered to support the view that the augmented lytic activity was due to differentiation of new killer cells in culture. These findings enabled demonstration of killer cells against a variety of syngeneic tumors in situations where no such reactivity was demonstrable before culture.

Additionally, novel methods of calculating the incidence of killer cells in lymphocyte populations and of characterizing the affinity of effector cells for homologous target cells have been reported and allow a more quantitative appraisal of data generated in cell-mediated cytotoxic assays than had previously been possible.

Significance to Cancer Research: This contract was aimed at increasing the sensitivity and quantitativeness of a common *in vitro* cytotoxic assay. Such studies may eventually result in an assay system that would allow a patient's immunological status with respect to his tumor to be correlated with his clinical progress.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Groups: Committee on Cancer Immunodiagnosis
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: New In Vitro Techniques to Evaluate Cell-Mediated Immunity to Intact Tumor Cells

Principal Investigator:	Dr. John T. Harrington
Name/Address	University of Texas Medical School
Performing Organization:	San Antonio, TX

Contract Number: N01-CB-43893
Starting Date: 6/1/74 Expiration Date: 10/31/77

Goal: To establish methods for measuring the cell-mediated immune response of tumor patients to their tumor antigens.

Approach: To develop and apply the agarose droplet micromethod for measuring cell migration inhibition -- an in vitro correlate of cell-mediated immunity -- in patients with bladder, lung, and breast carcinoma using antigens derived from autologous tumor material and from established tumor cell lines.

Progress: This research is being conducted in three overlapping phases: (1) Development of the agarose droplet method using a murine tumor allograft rejection model. These studies, which have been completed, permitted rapid technical development of the method and verification of its use for testing immunity to cell surface antigens. Cell freezing techniques, antigen extraction methods, and definition of the cell-mediated response in this model were also accomplished. (2) Development of a human agarose droplet micromethod. This work, which has been completed, tested the migration inhibition response of human tuberculin-sensitive individuals to PPD. Human assay conditions have been verified and optimal migrating indicator cells chosen. (3) Application of the micromethod to assess human tumor immunity. These studies are now in progress and have demonstrated positive migration inhibition reactions in bladder, lung, and breast carcinoma patients to extracts of tumor extracts of cultured cell lines derived from these tumors. Further definition of the specificity, reproducibility, and clinical correlation of these reactions are in progress.

Significance to Cancer Research: The accurate assessment of antitumor immunity in cancer patients may be important to both diagnostic and treatment decisions. Development of appropriate methods is critical to this effort.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $81,842

CONTRACT RESEARCH SUMMARY

Title: Isolation and Tissue Culture of Human Tumor Cells

Principal Investigator: Dr. Jorgen E. Fogh
Name/Address Sloan-Kettering Institute for Cancer
Performing Organization: Research
New York, NY

Contract Number: NO1-CB-43854
Starting Date: 8/8/73 Expiration Date: 8/7/77

Goal: To further develop procedures for encouraging tumor cell growth in culture and to perform tests to determine if cells in culture are indeed neoplastic rather than normal cells. To make cultures available to other investigators.

Approach: Human tumor cell lines are established in culture from surgical specimens and are collected from other investigators. They are characterized in this laboratory as to malignancy, cell type, and special features as needed for individual investigations.

Progress: Three hundred ninety established cell lines, derived from human tumors, have been collected from cultures. The experience gained during the past period permits cell line establishment from certain types of tumors much more frequently than in the past. Methods have been employed to assess malignant characteristics of the cultured cells, consistency in terms of tumor cell type with the tumor of origin, and special features of the individual cell lines. These methods have provided information on cell morphology, nutritional requirements, growth in vitro, tumor production in the nude mouse, chromosomal characteristics, poliovirus susceptibility, and isozyme patterns. Only a small proportion of the collected lines are suspected of HeLa cell contamination. Mycoplasmas and other contaminants of a number of the lines have been eliminated from all but 13 lines, still mycoplasma contaminated. The major part of the lines, and many early cultures, are frozen in liquid nitrogen and, when sufficiently characterized, available for distribution to collaborating investigators. A computerized catalog of clinical background information and cell characterization data is being constantly updated. A computerized data file of all cell specimens stored in liquid nitrogen has been established during the last year. One thousand seven hundred forty-four cultures of a variety of human tumor cell lines were shipped to investigators in the United States and abroad. Efforts are made to obtain data derived from their studies.

Significance to Cancer Research: The collection of well-characterized contamination-free human tumor cell lines is pertinent for many disciplines of experimental and clinical cancer research.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program Site Visit Date: 10/31/73
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 76 Funds: $224,000 (TQ)

CONTRACT RESEARCH SUMMARY

Title: Isolation and Characterization of Human Peripheral Blood Mononuclear Cells

Principal Investigator:	Dr. Stuart Schlossman
Name/Address	Sidney Farber Cancer Institute
Performing Organization:	Boston, MA

Contract Number: NO1-CB-43964
Starting Date: 5/16/74 Expiration Date: 5/15/78

Goal: Development of procedures for more effective and reproducible fractionation of mononuclear cells from human peripheral blood.

Approach: Peripheral blood from normal individuals and from patients with carcinomas will be studied. The following cell types will be isolated in suspension with high yields, purity, and viability: T lymphocytes, B lymphocytes, and monocytes. The isolated cells will be characterized for viability, morphology, retention of membrane markers, and retention of immunological functions.

Progress: The contractor has focused on identification of surface membrane determinants on human lymphocyte subpopulations analogous to TL, Ly, theta, and Ia determinants present on murine lymphocyte subpopulations. The analysis of surface determinants has aided work on the development of new techniques for the isolation of highly purified subclasses of human lymphocytes and permitted development of new in vitro techniques to discriminate the functional behavior of the isolated subclasses. Studies have also been done on human B cells, specifically analysis of the signals required for B-cell differentiation and control of that differentiation by T cells. Progress has been made on analysis of the role of human Ia-like determinants on the surface of lymphocytes and monocytes in the generation of cell-mediated immune responses.

Significance to Cancer Research: NCP Objective 5 Approach 1

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $81,663

CONTRACT RESEARCH SUMMARY

Title: Improvement of Methods for Isolation and Preservation of Lymphocytes

Principal Investigator: Name/Addresses Performing Organization:	Dr. Stuart Schlossman Sidney Farber Cancer Institute Boston, MA

Contract Number: N01-CB-43885
Starting Date: 5/16/74 Expiration Date: 5/15/77

Goal: To define techniques for the isolation of individual subsets of human lymphocytes which are viable and functionally intact, and to attempt cryopreservation of such lymphocyte subsets with the view of recovery and preservation of their functional properties.

Approach: The subsets of lymphocytes were assayed for structural integrity and viability, and analyzed *in vitro* by functional assays. Cell surface properties were defined before and after cryopreservation by three markers which have been particularly useful in this laboratory and included FITC-Fab anti-F(ab), aggregated gammaglobulin for Fc receptors, and anti-Ia-antisera.

Progress: The contractor concentrated in the past year on analyzing functional properties of lymphocytes and the effect of varying conditions in freezing and thawing on the recovery of subsets of lymphocytes, particularly the $Th1^+$ subset of human T cells capable of responding in MLC and the $Th1^-$ subset of lymphocytes which express cytotoxic activity. Attempts to change conditions which lead to a diminished viability of the recovered cell population severely affect ADCC activity. In addition, Fc binding was analyzed, concentration of Ia antigen and surface immunoglobulins on 40 individuals with CLL and following freezing and thawing. No changes in the surface properties of the cells were obtained by storage upwards of one year, and conditions affecting viability and recovery had little or no effect on the cell surface properties of the cells. Diminished total viability could be circumvented by recovery of cells following Ficoll-Hypaque centrifugation. No specific enrichment or deletions of effector functions were seen following cryopreservation.

Significance to Cancer Research: The cryopreservation of lymphocytes is important since it permits the recovery of populations of cells of defined structural and functional integrity for studies of immune responsiveness of cancer patients as well as to allow exchange among laboratories of defined populations of cells.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 76 Funds: $44,649 (TQ)

CONTRACT RESEARCH SUMMARY

Title: Isolation and Characterization of Human Peripheral Blood Mononuclear Cells

Principal Investigator:	Dr. Hans Wigzell
Name/Address	Uppsala University
Performing Organization:	Uppsala, Sweden

Contract Number: N01-CB-43883
Starting Date: 6/25/74 Expiration Date: 6/24/77

Goal: Human peripheral blood mononuclear cells constitute a population of cells, morphologically in a superficial way looking alike but with highly distinct immune functions. To separate and define such populations constitutes our major goal.

Approach: Development of surface markers, preferentially of a unique character signifying a given subgroup of cells, is the most ultimate approach allowing rapid fractionation and purification of blood mononuclear cells. A battery of fractionation procedures linked up with functional tests was applied in order to analyze this question.

Progress: It has been possible to develop a most sensitive and quantitative technique for the detection of membrane-associated IgG or antigen-molecules using iodinated protein A. Using this technique subsequently the Fc receptor distribution of subgroups of human blood mononuclear cells was analyzed, as well as HLA, and beta 2-microglobulin distribution pattern. Whereas striking differences exist in Fc distribution patterns, HLA and beta 2-microglobulin distribution profiles are very similar between subgroups. Protein A has also been found to be a human B-cell mitogen, a useful marker for blood B cells in man. New techniques have been developed as to allow simple fractionation of C3-receptor-bearing cells using C3-coated zymosan-particles. Helix pomatia A agglutinin can be shown to serve as a useful marker in the selective separation of T lymphocytes as well as natural killer cells. Specific analysis of separated subpopulations of human mononuclear cells labeled as to surface glycoproteins using sodium borohydride techniques indicates the existence of distinct subtype-specific glycoproteins. Antisera against such "bands" are being induced.

Significance to Cancer Research: Human peripheral blood constitutes a major, simple source of human mononuclear cells. Understanding this complex population as to surface markers as well as functional capacity is directly related to understanding how the immune system in that individual may function.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: 0

CONTRACT RESEARCH SUMMARY

Title: Isolation and Characterization of Human Peripheral Blood Monocytes

Principal Investigator: Name/Address Performing Organization:	Dr. David Talmage University of Colorado Medical Center Webb-Waring Lung Institute Denver, CO

Contract Number: N01-CB-53900
Starting Date: 5/16/75 Expiration Date: 5/15/78

Goal: To isolate monocytes from human peripheral blood, both from normal donors and from donors having carcinomata, and to test these cells for functional activity and markers.

Approach: Mononuclear cells are being separated from whole blood; monocytes are then isolated from the lymphocytes by counterflow centrifugation using a specially designed chamber.

Progress: Highly pure populations of monocytes, and also of lymphocytes, are being obtained by the described approach. Purity now averages about 95%. It should be noted, however, that it is not possible to separate all monocytes from all lymphocytes, a mixed population being obtained between the pure fractions. Normal monocytes defined by these assays have a bimodal volume spectrum, preventing their separation from the lymphocytes. In addition to phagocytic ability and peroxidase activity, the isolated monocyte populations are being tested for their role in the stimulation of lymphocytes by Con A. In normal donors, monocytes are an absolute necessity for stimulation when the culture includes homologous plasma. Furthermore, the degree of stimulation appears to be a linear function of the percentage of monocytes present at least up to a monocyte-lymphocyte ratio of 40%. Even at this level, however, stimulation is much less marked than for cultures which use FCS instead of homologous serum. In studies with cancer patients, it was found that phagocytosis is often, though not always, impaired, that peroxidase activity is very variable, and that cell volume spectrum is usually bizarre.

Significance to Cancer Research: The monocyte is known to play an important role in the immune system through its ability to stimulate lymphocytes. Dysfunction of the immune response in cancer can therefore be examined by comparison of experiments using monocytes isolated from normal donors and cancer patients.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $51,528

CONTRACT RESEARCH SUMMARY

Title: Purification of Human Tumor-Associated Antigens

Principal Investigator: Name/Address Performing Organization:	Dr. Ralph A. Reisfeld Scripps Clinic and Research Foundation La Jolla, CA

Contract Number: NO1-CB-53899
Starting Date: 6/1/75 Expiration Date: 5/31/78

Goal: Development of new methods for the purification and physicochemical characterization of human tumor-associated antigens and to make them available for cell-mediated immunity assays and for diagnostic testing.

Approach: Human melanoma-associated antigens (MAA) are isolated by mild, least denaturing procedures from fresh tumor tissues and from cultured melanoma cells and their spent culture media derived from the same melanoma patients. This includes removal of HLA antigens and purification and physicochemical characterization of MAA which are defined biologically by their ability to elicit specific delayed cutaneous hypersensitivity reactions in melanoma patients.

Progress: Human melanoma-associated antigens (MAA), when solubilized from cultured tumor cells by extraction with 3M KCl, were shown to be antigenic and elicited a cell-mediated immune reaction as determined by delayed cutaneous hypersensitivity responses (DCHR). Between 75-80% of melanoma patients showed positive DCHR, while only 25% of patients with other neoplasms reacted. Antigen purification was achieved by KBr gradient ultracentrifugation, cellulose (DEAE), ion-exchange chromatography, and preparative isoelectric focusing (IEF) on Pevikon C870. A new method was developed to remove histocompatibility antigens as well as lipids and lipoproteins from MAA utilizing KBr gradient ultracentrifugation. Several in vitro antibody-binding assays developed in our laboratory were utilized to assess their potential to quickly evaluate the progress of antigen purification.

Significance to Cancer Research: The continuous availability of chemically and biologically defined purified human melanoma-associated antigens should prove advantageous to establish their utility to produce specific xenoantibody and to test the efficacy of these reagents for tumor diagnosis, therapy, and in monitoring response to therapy.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $160,931

CONTRACT RESEARCH SUMMARY

Title: Purification of Human Tumor-Associated Antigens

Principal Investigator: Name/Address Performing Organization:	Dr. Arthur Malley Oregon Regional Primate Research Center Beaverton, OR

Contract Number: N01-CB-53954

Starting Date: 6/16/75 Expiration Date: 6/15/78

Goal: Isolate homogenous preparations of tumor-associated antigens from human melanoma and squamous cell carcinoma tissue in sufficient quantity to permit biological and chemical characterization.

Approach: Tumor tissue is extracted, purified, and tested for the presence of tumor-specific antigens by dermal skin tests and leukocyte adherence inhibition.

Progress: The optimal conditions were explored for the extraction of melanoma tumor-specific antigens from melanoma tissue. A wide variety of reagents were evaluated, and 4M KCl provided the maximum release of melanoma tumor antigens. An in vitro method (leukocyte adherence inhibition assay) was developed for detecting tumor-specific melanoma antigens. The specificity of the LAI assay was examined by testing various tumor extracts with leukocyte suspensions of tumor patients and normal healthy donors. A linear relationship exists between the concentration of protein in a melanoma extract giving a 10 mm indurated skin reaction and the concentration of protein giving a maximum LAI reaction. A melanoma antigen fraction was obtained containing two to six bands on polyacrylamide disc electrophoresis and a 2000-fold increase in tumor-specific melanoma antigen activity. Of interest is the observation suggesting that a relationship might exist between melanoma antigens and human β_2-microglobulin: significant amount of melanoma antigen activity was bound to a Sepharose-anti β_2-microglobulin adsorbent and eluted with 3M NaSCN. Further testing will involve the blocking of melanoma antigen binding to the adsorbent by pretreatment of the adsorbent with purified β_2-microglobulin.

Significance to Cancer Research: The availability of pure tumor antigens will provide a reagent that will permit the development of sensitive in vitro radioimmunoassays for the early detection of tumor antigen. In addition, the structural characterization of these pure tumor antigens may provide some insight on how tumor antigens escape the immune apparatus of the host.

Project Officer: Mrs. Judith Whalen

Program: Tumor Immunology Program Site Visit Date: 5/21/76

Technical Review Group: Committee on Cancer Immunodiagnosis

FY 77 Funds: $77,248

CONTRACT RESEARCH SUMMARY

Title: Purification of Human Tumor-Associated Antigens

Principal Investigator: Name/Address Performing Organization:	Dr. George L. Wright Eastern Virginia Medical Authority Norfolk, VA

Contract Number: NO1-CB-53955
Starting Date: 6/30/75 Expiration Date: 6/29/78

Goal: To isolate, purify, and identify human tumor-associated antigens.

Approach: Isolate and purify tumor-associated antigens from crude tumor extracts of urogenital tumors and test them for functional activity in assays of humoral and cell-mediated immunity.

Progress: Extracts prepared from renal cell carcinomas and other urogenital tumors were tested for antigenic activity using the leukocyte migration inhibition test. Many of the extracts tested demonstrated little activity or specificity. One renal carcinoma extract was found to be reactive and adequately discriminated between renal carcinoma patients, normal donors, and patients with other types of cancer. Sixty-three percent of the patients with renal carcinoma and only 7% of the normal donors and 30% of patients with other cancers were positive. The reactivity appeared specific since only 20% of the renal carcinoma patients reacted to a normal kidney extract. Additional testing showed that some renal carcinoma patients gave positive tests to a lung cancer extract; the nature of this cross-reactivity has yet to be determined. A tumor-associated antigen was partially purified from the crude renal carcinoma extract and was demonstrated to be slightly increased in both activity and specificity.

Significance to Cancer Research: The availability of purified and well-characterized tumor antigens would greatly facilitate the development of more sensitive immunodiagnostic tests for the screening and management of the cancer patient.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $77,283

CONTRACT RESEARCH SUMMARY

Title: Role of Antibody-Dependent Cell-Mediated Cytotoxicity in Tumor Immunity

Principal Investigator: Dr. Osias Stutman
Name/Address: Sloan-Kettering Institute for Cancer Research
Performing Organization: New York, NY

Contract Number: N01-CB-53894
Starting Date: 5/1/75 Expiration Date: 4/30/78

Goal: Determine the importance of cytotoxicity of syngeneic tumor cells by antibody-dependent cell-mediated mechanisms in host resistance to tumor growth or spread, and whether the presence of such antibodies would be useful for the detection of malignant or premalignant lesions and for monitoring tumor growth.

Approach: Study the role of antibody-dependent cell-mediated cytotoxicity in tumor immunity in a mouse syngeneic system using spontaneous mammary adenocarcinomas.

Progress: A reliable assay for antibody-dependent cell cytotoxicity (ADCC) using a syngeneic mouse system was developed. The antibody has activity in IgG subclasses and not in IgA or IgM and it is thymus dependent in development. The antibody is produced by hyperimmunization with mammary tumor cells or derived from tumor-bearing C3H mice. Adherent C3H mammary tumors prelabeled with ^{3}H-proline are target cells. Effector cells are from normal C3H or C3Hf donors. Effector cells are relatively radioresistant (especially those derived from blood or peritoneal cavity; those from spleen are less sensitive); treatment of the donors with ^{89}Sr does not affect the spleen cell effectors; concerning surface markers, the effector cell is negative for all T markers while B-specific markers reduce their effectivity. The *in vitro* responses can be inhibited by relevant free antigen, excess free specific antibody, excess free irrelevant soluble Ig, aggregated or insoluble Ig, and relevant or irrelevant antigen-antibody complexes.

Significance to Cancer Research: (NCP Objective 6 Approach 4 and Objective 3 Approach 4)
Studies of cells involved in the immune destruction tumors are an important part of Baseline Information Flow in the Tumor Immunology Program.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $66,744

CONTRACT RESEARCH SUMMARY

Title: Development of Macrophage Electrophoretic Mobility Assay for Malignant Disease

Principal Investigator: Dr. Leonard Weiss
Name/Address
Performing Organization: Health Research, Inc.
Roswell Park Memorial Institute
Buffalo, NY

Contract Number: NO1-CB-53901
Starting Date: 6/1/75 Expiration Date: 5/31/78

Goal: Investigation of the macrophage electrophoretic mobility assay as a valid tool in the diagnosis and monitoring of malignant disease.

Approach: Establishment of the assay and refinement of cell preparation and electrophoresis techniques. Preparation of data in such a way as to allow direct comparison of results among independent investigators. Examination of series of patients with various clinically confirmed and staged cancer, including premalignant lesions, together with appropriate controls. Exploration of the biologic basis of the assay using experimental animals bearing tumors or challenged with conventional antigens. Performance of the assay on a "blind" trial basis with coded specimens organized by NCI.

Progress: The assay has been refined and performed on a series of patients with clinically confirmed colorectal cancer and controls. The test gave positive results in a high percentage of patients, but approximately 30% of apparently healthy controls also gave positive results. A series of patients with melanoma is currently being examined with positive results in a large majority of cases. A second series of assays on patients with premalignant and malignant skin lesions during the course of their treatment has been initiated. Patients with a history of cutaneous malignancy, where progress following treatment is currently being monitored, are also being examined and greater than 95% gave positive results. "Blind" trial studies with coded specimens organized through NCI have been started. Preliminary studies with experimental animal model systems have so far only indicated the possibility of a more universal biologic application of the assay.

Significance to Cancer Research: This assay could be potentially useful in monitoring the clinical status of patients with, or with a history of, cancer rather than in initial detection of the disease. It could also provide a method of examining the apparently important role played by macrophage-lymphocyte-tumor interactions in the progress of malignant disease.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $39,199

CONTRACT RESEARCH SUMMARY

Title: Development of Macrophage Electrophoretic Mobility Assay for Malignant Disease

Principal Investigator: Dr. John A. Pritchard
Name/Address Velindre Hospital
Performing Organisation: Whitchurch, Cardiff, Wales

Contract Number: NO1-CB-53956
Starting Date: 6/29/75 Expiration Date: 9/29/77

Goal: The use of a biochemical technique to isolate and identify an effector compound released by cancer-sensitized lymphocytes, or by stimulation with appropriate antigen; development of a refined apparatus for the measurement of macrophage mobility in the bioassay for the presence of the effector compound. Where possible, both systems to be appraised by a series of coded blood samples to establish the clinical value of the macrophage electrophoretic mobility (MEM) test for malignant disease.

Approach: Large-scale preparation of the effector compound, macrophage slowing factor (MSF), to be undertaken. The active fractions to be pooled (by ultrafiltration) and used to raise a rabbit anti-MSF serum. Assessment of the rank Mk.III electrophoresis system for the simple measurement of macrophage mobilities.

Progress: The mediator of macrophage slowing (MSF) has been found to have a molecular weight of 20-23,000 and this is consistent with published data. It is stable at 56°C and a storage (4 weeks) at -10°C. Bioassay, using macrophage mobility reduction, showed that activity was retained at 10^{-5} dilution. Conventional means of biochemical analysis could not establish its presence. Repeated attempts using up to 50 individual lymphocyte preparations to produce MSF, which was subsequently pooled and ultrafiltered, were unsuccessful in raising an antisera. The rank Mk.III electrophoresis system has been developed for ease of operation in the measurement of all mobilities and has been assessed in the operation of the MEM assay and found to produce similar results as obtained with the Zeiss cytopherometer with considerably less operator fatigue. Results on a coded series of 240 samples are in the process of analysis.

Significance to Cancer Research: The MEM test has been proposed as a sensitive laboratory test for malignant disease. This can only be truly assessed in the routine operation of the test in conjunction with accepted clinical procedures.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 76 Funds: $6,618 (TQ)

CONTRACT RESEARCH SUMMARY

Title: Diagnostic Application of Human Tumor-Associated Antigens

Principal Investigator:	Dr. Calvin A. Saravis
Name/Address	Mallory Institute of Pathology
Performing Organization:	Boston, MA

Contract Number: NO1-CB-64071
Starting Date: 6/16/76 Expiration Date: 5/31/78

Goal: To develop an assay system for the tumor marker, ZGM, that is useful in the diagnosis and management of digestive tract malignancy.

Approach: To develop a sensitive radioimmunoassay for detecting ZGM in the blood of patients with gastrointestinal cancer; use of immunofluorescence microscopy to detect ZGM in surgical and biopsy specimens for histopathological diagnosis and prognosis; to correlate the results of the presence of ZGM in blood and its detection in histological sections with the presence or absence of malignancy.

Progress: ZGM was detected in primary and metastatic colon cancer and was not detected in normal human plasma, normal colon, normal liver, and normal spleen. It was distinct from CEA, from antigens cross-reacting with CEA, AFP, alpha-2 macroglobulin, ferritin-like molecules, blood group antigens, and buffy coat. During the present contract year purified ZGM and avid, high-titer anti-ZGM antisera were produced. A ZGM radioimmunoassay is being developed. Immunofluorescence microscopy was used for selecting the ZGM-positive tumors from which ZGM was isolated. Thirty-four of 39 colon adenocarcinomas, 6 of 6 gastric adenocarcinomas, and 0 of 20 non-G.I. carcinomas were ZGM positive. In addition, ZGM was detected in the lymphatic-containing tumor draining the primary tumor.

Significance to Cancer Research: The detection of the ZGM in patient specimens may permit earlier diagnosis, better evaluation of prognosis and monitoring of therapy for cancer.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $91,071

CONTRACT RESEARCH SUMMARY

Title: Clinical Evaluation of Immunodiagnostic Tests for Cancer

Principal Investigator: Name/Address Performing Organization:	Dr. Maria Linder California State University Fullerton, CA

Contract Number: NOI-CB-74119
Starting Date: 11/1/76 Expiration Date: 10/31/77

Goal: Ceruloplasmin (CP) is a copper-containing α_2-glycoprotein of plasma with enzymatic activity. The activity and concentration of CP are elevated in animals with tumors and in humans with lung cancer. The goal of this contract is to determine whether this phenomenon prevails for humans with other kinds of cancer and whether tests of CP would be useful in early diagnosis, for prognosis, or in treatment of the disease.

Approach: The primary approach is to measure CP antigen concentration, enzyme activity, and plasma copper concentrations in large panels of sera from cancer patients and controls, examining different kinds of cancer, different stages of the disease, patients before and after treatment of recurrence, and, in the case of lung cancer, heavy smokers who may develop the disease.

Progress: In initial studies of lung cancer patients, a clear relationship between the degree of CP (and Cu) elevation and disease stage was noted: after successful therapy levels return to normal; after surgery, generally but not always, CP and Cu levels decrease; patients who develop a recurrence maintain higher than normal levels of CP after primary treatment. Irradiation and chemotherapy have different effects in different individuals, and further evaluation is required. Sera from breast cancer patients show even higher levels of CP than those with lung cancer in initial studies. In soluble extracts of normal and malignant human tissues immunological and enzymatic evidence was obtained for the presence of CP in amounts which could not be accounted for by residual blood. The possibility that cultured human lung tumor cells secrete CP into the medium is now being investigated.

Significance to Cancer Research: Potentially, this project is of great significance in that it may offer a chemical/immunological serum test for gauging cancer stage and size, a means of early diagnosis for several forms of cancer, and a way of judging the success of therapy, and following the course of the disease. It may also offer a fundamental insight into the metabolism of tumor cells.

Project Officer: Mrs. Judith Whalen
Program: Tumor Immunology Program
Technical Review Group: Committee on Cancer Immunodiagnosis
FY 77 Funds: $28,435

NCI GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 19659

TITLE: Aryl Hydrocarbon Hydroxylase Levels: Head-Neck Cancer

PRINCIPAL INVESTIGATOR: Lawrence J. Alfred

INSTITUTION: Charles R. Drew Postgraduate Medical School
Los Angeles, CA

ABSTRACT: One of the earliest, if not the primary, responses of cultured normal animal cells to treatment with polycyclic hydrocarbons (PH) is the induced synthesis of aryl hydrocarbon hydroxylase (AHH). AHH is a multicomponent membrane-bound monooxygenase which requires NADPH and molecular oxygen for the metabolism of certain exogenous substrates such as carcinogenic PH. The induction of AHH in mouse cells in vitro and in vivo, and in cultured human lymphocytes appear to be genetically controlled. Based on AHH activity in lymphocyte cultures, human subjects fall into three inducible groups (low, intermediate, high), and healthy persons with high AHH inducibility may have a greater propensity for developing lung cancer; 30% of patients with bronchogenic carcinoma fall into the high group, while only about 9% of healthy subjects fall into the high group. Thus, responsiveness of human lymphocytes to AHH induction appears to be related to a genetic variability in the occurrence of lung cancer. A relationship between lymphocyte AHH activity and other types which might arise from respiratory epithelium has not been shown. To test this hypothesis, we will determine whether cultured lymphocytes derived from adult patients with demonstrated carcinoma of the head and neck region have statistically higher levels of AHH than lymphocytes from healthy controls. This type of malignancy was chosen for the proposed study because of its cellular origin, which in some cases is respiratory epithelium; it is one of the first tissues exposed to inhaled or ingested environmental carcinogenic chemicals; and because this tumor is usually detected as primary. The immediate objectives of the proposed study are: (1) to measure the induced AHH activity in cultured lymphocytes from the peripheral blood of adult patients with head and neck cancer, and from healthy control subjects; (2) to determine the rates of proliferation of the above lymphocyte culture systems; (3) to isolate and identify the T and B lymphocytes from healthy and cancer subjects, and compare the AHH activity in both cell populations. The long range goal of this study is to develop a reproducible cell culture system to determine man's potential susceptibility to toxic and carcinogenic environmental chemicals.

NCI GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 18404

TITLE: Histaminase and Amines in Neutral Crest Tumors

PRINCIPAL INVESTIGATOR: Stephen B. Baylin

INSTITUTION: Johns Hopkins University
Baltimore, MD

ABSTRACT: The project in progress explores the relationship of biogenic amines to certain endocrine tumors and tumors with endocrine function in two ways. Firstly, the amine metabolizing enzyme, histaminase (diamine oxidase), which is found in medullary thyroid carcinoma, is being extensively studied in this tumor, and in other tumors which may be embryologically related. Methods for rapid and high degree purification of the enzyme have been developed. Purified histaminase from human placenta is being compared (substrate specificity, electrophoretic mobility, amino acid content, and antigenicity) to histamine in medullary thyroid carcinoma, small cell carcinoma of the lung, human kidney and intestine, and rat thymus, intestine and adrenal glands. Through such comparisons it is hoped that the expression of this enzyme activity by certain tumors will be better understood.

Secondly, the effect of amines such as dopamine, norepinephrine and serotonin on peptide-hormone release from tumors capable of endogenous synthesis of these amines is under investigation. In vivo and in vitro studies of calcitonin release from medullary thyroid carcinoma tissue are being used for this purpose. Release of this hormone under conditions of added amine precursors in the presence and absence of blockade of biogenic amine synthesis is being explored.

NCI GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 16563

TITLE: Serum Tyrosinase in Malignant Disease

PRINCIPAL INVESTIGATOR: Yu M. Chen

INSTITUTION: Wayne State University
Detroit, MI

ABSTRACT: The major aims of the proposed study are to assess specifically the tyrosinase activity and its electrophoretic patterns in the serum of patients with malignant diseases, to study the dissociation-association of the serum tyrosinase carrier and the enzyme and to explore a possible immunological aspect of the serum tyrosinase carrier. The proposed research is expected to provide specific information concerning serum tyrosinase to be utilized for both diagnosis and immunotherapy of malignant disease or diseases.

The specific determination of serum tyrosinase activity and fair demonstration of its electrophoretic pattern from an isolated serum fraction are already available. The dissociation-association of the serum tyrosinase carrier and the enzyme and the immunological aspect of the serum tyrosinase carrier can be initiated and approached by utilization of lipase digestion and many promising biochemical techniques.

NCI GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 18863

TITLE: Monitoring Familial Medullary Carcinoma of the Thyroid

PRINCIPAL INVESTIGATOR: Myron Genel

INSTITUTION: Yale University
New Haven, CT

ABSTRACT: Medullary carcinoma of the thyroid is an aggressive neoplasm of the parafollicular cells which results in excessive secretion of thyrocalcitonin. The objective of the study is to devise a reliable, comprehensive plan to follow a kindred of 127 patients, half of whom are at risk to develop medullary carcinoma of the thyroid, in an effort to identify patients with premalignant lesions. These patients will be followed with calcium infusion tests, urinary catecholamines and physical examinations.

NCI GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 19164

TITLE: DNA Polymerase Inhibitor in Sera of Tumor-Bearing Hosts

PRINCIPAL INVESTIGATOR: A. Arthur Gottlieb

INSTITUTION: Tulane University
New Orleans, LA

ABSTRACT: Characterization of an inhibitor of DNA polymerase found in sera of patients with certain malignancies.

NCI GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 17563

TITLE: DNA-Binding Proteins in Human Serum

PRINCIPAL INVESTIGATOR: Sallie O. Hoch

INSTITUTION: Scripps Clinic and Research Foundation
La Jolla, CA

ABSTRACT: Proteins that function in association with DNA have been extensively investigated in prokaryotic and eukaryotic systems because of their possible regulatory roles. We have used the technique of affinity chromatography on DNA-cellulose to isolate a class of DNA-binding proteins from human serum. These proteins appear to be unique among the serum proteins and comprise a significant fraction (1.5 percent) of these proteins. We propose to determine the physiological function(s) of the DNA-binding proteins by a combination of biochemical and clinical studies. Our first objective is to characterize the two major DNA-binding protein species in normal serum; these proteins have been purified to homogeneity. Their characterization includes determination of physical and chemical properties by conventional techniques; determination of substrate specificity using a nitrocellulose membrane filter assay; determination of function including the use of an *in vitro* transcription system using human chromatin as template; development of radioimmunoassays for these proteins to facilitate the screen for genetic polymorphism in the general population. Our second objective is to continue the characterization of a malignancy-associated DNA-binding protein. This protein's characterization includes determination of physical and chemical properties to explore its relationship to complement component C3; extensive use of a screening procedure and radioimmunoassay to definitively determine its potential as a prognostic and/or diagnostic indicator; exploration of the role of serum proteases in producing this protein and possibly others of the DNA-binding proteins.

NCI GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 18954

TITLE: Biochemical Markers of Malignancy

PRINCIPAL INVESTIGATOR: Marvin A. Kirschner

INSTITUTION: Newark Beth Israel Medical Center
Newark, NJ

ABSTRACT: Among the many examples of ectopic hormone production by tumors, the gonadotropin (HCG)-producing neoplasms may represent a unique phenomenon of tumor retro-differentiation. Previous studies have shown these tumors to make not only HCG and/or its alpha and beta fragments, but also to elaborate somatomammotropin and placental alkaline phosphatase. These tumors thus appear to have de-differentiated to perform the same biochemical functions of normal placenta and trophoblastic neoplasms.

Previous studies from our laboratory have shown that normal placenta and trophoblastic tumors are capable of aromatizing circulating androgens, particularly dehydroepiandrosterone sulfate, to estradiol. Since this steroid transformation cannot be demonstrated in normal (non-pregnant) states, elevated estradiol production from this pathway can serve as a useful biochemical marker of trophoblastic neoplasms. We have also studied estrogen production rates and DHEA-SO_4 conversion to E_2 in patients with ectopic HCG-producing neoplasms and found these elevated. Thus, we feel that ectopic estradiol production by tumor tissue represents another biochemical feature that characterizes functioning trophoblastic tissue, suggesting that these tumors represent an unusual form of tissue retro-differentiation.

In the current proposal, we wish to examine estradiol production rates as well as other trophoblastic markers in cancer patients found to have ectopic HCG beta fragments in their serum. We hope to demonstrate that these neoplasms producing HCG beta also perform other biochemical functions characteristic of trophoblastic tissue and thus represent an unusual syndrome vs. other ectopic hormonal syndromes where only a single repressed protein and/or its fragments are made by the tumor tissue.

NCI GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 15515

TITLE: Polyamines and Brain Tumor Chemotherapy

PRINCIPAL INVESTIGATOR: Laurence J. Marton

INSTITUTION: University of California
San Francisco, CA

ABSTRACT: To correlate the synthesis of polyamines with tumor cell proliferation *in vitro*. Polyamine metabolism will be related to different tumor cell types including clones. Using techniques to achieve cell cycle synchronization and/or produce phase arrest, the synthesis of polyamines will be related to cell cycle kinetics.

To determine polyamine levels in blood, urine, cerebrospinal fluid and tumor tissue and the level of their biosynthetic enzymes in rats and mice bearing transplanted brain tumors. Animal models will also provide a tool for investigating the potential for polyamine antimetabolites as oncolytic agents.

To study polyamines in patients bearing brain tumors before and during radiotherapy and chemotherapy. Polyamines will be determined in cerebrospinal fluid, blood and urine, and these values will be correlated with operative specimens and tumor cyst fluid, tumor type and grade, and either progression or regression of a tumor during treatment using clinical criteria.

NCI GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 17353

TITLE: Marrow Culture Studies -- Human Myeloid Leukemia, Etc.

PRINCIPAL INVESTIGATOR: Malcolm A. Moore

INSTITUTION: Sloan-Kettering Institute for Cancer Research
New York, NY

ABSTRACT: The project has two major objectives. The first is the application of the agar culture technique for detection of quantitative and qualitative defects in granulocytic stem cells (CFU-C) in the marrow of patients with leukemia and myeloproliferative disorders in both the untreated phase and during the course of therapy. This screening protocol is designed to provide detailed information of diagnostic and prognostic value.

The second major objective evolves from this screening program and is aimed at investigating (1) the nature of the cellular and regulatory lesions in leukemia, and (2) the interaction between normal and leukemic hematopoietic cell populations during the development and treatment of the disease.

NC. GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 14783

TITLE: Polyamine Metabolism in Cancer and Cancer Chemotherapy

PRINCIPAL INVESTIGATOR: Diane H. Russell

INSTITUTION: University of Arizona
Tucson, AZ

ABSTRACT: We have set up an automated amino acid analyzer technique to quantitate putrescine, spermidine and spermine in the urine and serum of patients with breast cancer, multiple myelomas, lymphomas, and leukemias. The elevations detected in the urine and serum of cancer patients prior to chemotherapy are thought by us to reflect the spontaneous cell loss factor of the particular type of cancer. Those patients with carcinomas have the highest initial elevation of polyamines in serum and urine, and this is in agreement with the high spontaneous cell loss factor that occurs in carcinomas (i.e., up to 70%). In response to chemotherapy, there is a rapid increase in both putrescine and spermidine in the serum and urine. The elevation appears several hours earlier in the serum than in the urine, which would be expected, and starts to decrease prior to the decrease in urine polyamines. We are in the process of assessing whether the absolute increase can be correlated with the number of tumor cells that have been killed by the chemotherapy. It appears that an increase of over 2-fold in the spermidine concentration of serum occurs only in good responders, whereas poor responders never show increases of that magnitude. Many of the responders have elevations in spermidine that are 5- to 10-fold in both serum and urine. Attempts are being made at this time to find proper controls; i.e., good responders to chemotherapy (leukemia) vs. poor responders to chemotherapy (leukemia), good responders, lymphoma vs. poor responders, lymphoma, etc. It appears at this time that measurement of polyamines in serum and urine of cancer patients may indicate the current status of the tumor, and may be useful to assess clinical response to chemotherapy or radiation therapy. Research projects are also ongoing in an attempt to determine the nature of the conjugates of polyamines that occur in urine and serum.

NCI GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 21570

TITLE: Vasoactive Intestinal and Lung Polypeptides

PRINCIPAL INVESTIGATOR: Sami I. Said

INSTITUTION: University of Texas Health Science Center
Dallas, TX

ABSTRACT: We plan to investigate the incidence and effects of secretion by neoplasms of two recently identified vasoactive polypeptides: the vasoactive intestinal polypeptide (VIP), and a related vasoactive lung polypeptide. These peptides will be detected and measured by radioimmunoassay of plasma and tissues from normal (experimental animals, human subjects) and neoplastic lesions (human subjects), and by immunofluorescent staining of tissues. The findings will be analyzed for the possibilities of use of the peptides as markers for the presence of certain neoplasms, and their significance as mediators of paraneoplastic syndromes, especially "pancreatic cholera" flushing and hypercalcemia.

NCI GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 21518

TITLE: Radiation-Induced Thyroid Cancer

PRINCIPAL INVESTIGATOR: Arthur B. Schneider

INSTITUTION: Michael Reese Hospital and Medical Center
Chicago, IL

ABSTRACT: The major objective of this research proposal is to study radiation-induced thyroid cancer by a coordinated program of clinical and basic endocrinological investigations. The clinical studies are designed to determine the current risk and continuing incidence of radiation-induced thyroid cancer and to evaluate methods of diagnosis and medical and surgical approaches to treatment. This will be accomplished by a longitudinal study of patients who have been evaluated at Michael Reese Hospital because of a history of childhood head or neck irradiation. Of 5,200 patients who were so treated, 1,500 already have been examined and another 1,000 have been contacted by mail. Among those examined, a 31% prevalence of nodules was found, and among those who had surgery, a 32% rate of carcinoma was determined. Follow-up examinations of these patients will provide the information necessary to develop clinical guidelines for the care of persons with a history of head or neck irradiation.

Laboratory studies will focus on the role of plasma thyroglobulin in the diagnosis of thyroid tumors. Preliminary data showed that plasma thyroglobulin was elevated in many patients with thyroid nodules but that it was not suitable as a single screening procedure. Detailed studies of the molecular properties of plasma thyroglobulin will be undertaken in order to improve its diagnostic usefulness and to understand how it enters the circulation. In addition, an in vitro system will be used to determine at what point thyroglobulin is released from the thyroid into the circulation.

The early events in radiation-induced thyroid cancer formation will be studied by irradiating rat thyroid glands. The immediate and long-term effects of radiation in causing hormonal changes and tissue damage will be determined by sequential measurements of thyroglobulin, TSH and thyroxine. These effects will be correlated to the number of cancers formed, so that their role in thyroid cancer induction can be evaluated. The ability of thyroxine suppressive therapy to prevent cancer formation also will be tested in this system.

NCI GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 19000

TITLE: Colchicine-Sensitivity Test for Leukemic Lymphocytes

PRINCIPAL INVESTIGATOR: Robert Schrek

INSTITUTION: Northwestern University
Chicago, IL

ABSTRACT: *In vitro* studies have shown that non-dividing blood lymphocytes from patients with chronic lymphocytic leukemia are more sensitive than normal lymphocytes to the cytocidal action of many reagents including prednisolone, L-asparaginase, cytarabine, vincristine, and colchicine. As the maximum difference was obtained with colchicine, a pilot study was undertaken to consider the possibility of using this reagent as a test for leukemic lymphocytes. The method used for measuring sensitivity was by a special slide chamber and the counting of viable lymphocytes by phase contrast microscopy. The sensitivity was expressed as the average cytocidal effect produced by 1.0 and 0.1 microgram/ml of colchicine incubated with the cells at 37°C for 20 hours. A high degree of sensitivity of blood lymphocytes was observed for 18 patients with active chronic lymphocytic leukemia, and for 3 patients with presumptive early lymphocytic leukemia; low sensitivity was obtained for one leukemic patient in complete remission, and for 8 normal persons.

This possible diagnostic test will be evaluated by studies on treated and untreated leukemic patients, on leukemic patients in partial and complete remission and relapse, on non-leukemic patients with various types of lymphocytosis, and on normal persons. These studies are designed to determine the accuracy, specificity, limitation, and clinical usefulness of the colchicine-sensitivity test for leukemic lymphocytes. Work will also be done to modify and simplify the method of testing, to make it suitable for the clinical laboratory.

NCI GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 15169

TITLE: Blood Serum Glycosphingolipids and Malignancy

PRINCIPAL INVESTIGATOR: Vladimir P. Skipski

INSTITUTION: Sloan-Kettering Institute for Cancer Research
New York, NY

ABSTRACT: Objectives: (1) To elucidate the chemical composition of protein-lipid complexes of a proteolipid type, tentatively called neoproteolipids, isolated from malignant tumors; (2) to determine the degree of specificity of association of these complexes with malignant growth; (3) to investigate the appearance (or raised level) of these complexes in blood sera in order to serve as a potential diagnostic cancer test and/or as a test of the efficacy of the medical treatment of cancer.

Approach and Progress: From the lower phase of Folch-partitions of lipid extracts from tumors, protein-lipid complexes, neoproteolipids (NPL), have been isolated on systems of silicic acid chromatography columns. There are two types of NPL: Neoproteolipid-W (NPL-W), originally isolated from Walker carcinosarcoma 256 (W256), and neoproteolipid-S (NPL-S), originally isolated from sarcoma 180. Around 20 different transplanted, chemically induced and spontaneous tumors (including human tumors) were tested, and all of them contained either NPL-W or NPL-S. Both neoproteolipids are complexes of glycosphingolipids with other lipids (phospholipids, cholesterol) and proteins (or polypeptides). NPL-W contains neutral glycosphingolipids (which contain fucose), whereas NPL-S contains sialoglycosphingolipids as has been determined by gas-liquid chromatography. Blood sera of normal rats do not contain NPL-W, whereas the sera of W256-bearing rats do contain around 16 μg NPL-W/100 mg lipid. Blood sera from Morris hepatoma 5123-bearing rats contain 5-7 times more NPL-S than sera from normal rats. The presence of NPL (without identification of its type) was demonstrated also in sera of cancer patients with advanced forms of cancer.

NCI GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 13533

TITLE: Ectopic Placental Proteins in Human Cancer

PRINCIPAL INVESTIGATOR: Howard H. Sussman

INSTITUTION: Stanford University
Stanford, CA

ABSTRACT: The general problem with which we are concerned is the elucidation of cellular mechanisms of gene regulations which relate to the neoplastic process in humans. The phenomenon of ectopic protein synthesis in human cancer offers a good experimental model for investigating this problem. The ectopic synthesis of placental proteins by non-trophoblastic neoplasms is of special interest because of the frequent association of similar characteristics in neoplastic cells and embryonic cells. This has suggested that there may be a link between the mechanisms associated with the depression of the genes synthesizing embryonic proteins and those involved in neoplastic transformation. The investigation outlined in this proposal will make use of material obtained from clinical studies of patients manifesting evidence of ectopic synthesis of human chorionic gonadotropin and placental alkaline phosphatase. We plan to initiate experiments in two fundamental categories. (1) Proof of ectopia: These experiments are designed to test the assumption that the placental proteins are indeed synthesized by non-trophoblastic tumors and the assumption that they are coded for by the same genes as their normal counterparts. Chemical structure of the ectopic and placental proteins will be compared by several methods to determine whether they are the same. (2) Studies on the regulation of gene expression in normal and neoplastic cells: We plan to measure and compare patterns of synthesis of placental proteins in normal trophoblast, in choriocarcinoma and in non-trophoblastic tumors to determine whether similar regulatory mechanisms are operational. Initially these experiments will be performed in short-term tissue slice cultures from normal trophoblasts and from tumors which synthesize placental proteins ectopically. We plan to develop cell lines of these two tissues and to use these together with cell lines of choriocarcinoma which are already available to extend these experiments. We also plan to use cloned cell lines from the three sources to do cell hybridization.

NCI GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 19231

TITLE: An Improved Clinical Test for Prostatic Acid Phosphatase

PRINCIPAL INVESTIGATOR: Robert L. Van Etten

INSTITUTION: Purdue University
West Lafayette, IN

ABSTRACT: In contrast to all of the substrates currently being used to measure serum acid phosphatase levels as an aid in the diagnosis and confirmation of prostatic cancer, it appears that phosphoryl choline may have a truly unique specificity vis a vis hydrolysis by the prostatic enzyme. It is proposed to test this possibility in the clinical laboratory by making measurements of acid phosphatase levels in serum samples by one of the currently used conventional methods and also with the use of choline phosphate as a substrate. The results will be compared for the extent of correlation of the two methods with confirmed cases of prostatic cancer.

NCI GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 13447

TITLE: Circulating Thyroglobulin in Thyroid Carcinoma

PRINCIPAL INVESTIGATOR: Andre J. Van Herle

INSTITUTION: University of California
Los Angeles, CA

ABSTRACT: The present study is intended to evaluate the usefulness of the measurement of serum thyroglobulin in the patients with a potential differentiated malignant tumor of the thyroid gland. The study is also designed to establish whether serum thyroglobulin measurements can be used to evaluate the recurrence of tumor tissue (metastases) after the original malignant tumor was removed surgically. These data would allow optimalization of the care of these patients with reduction in complexity of the testing and costs of the tests involved.

NCI GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 16073

TITLE: Fetal Isoenzymes as Biologic Markers

PRINCIPAL INVESTIGATOR: Galen L. Wampler

INSTITUTION: Virginia Commonwealth University
Richmond, VA

ABSTRACT: The overall goal of the research project is to develop a profile of enzyme tests that will be useful for following the clinical course of cancer patients in the manner that other biologic markers such as HCG or CEA are currently being used.

Results to date indicate that enzyme changes occur within one week of administration of chemotherapeutic agents that would appear to be useful in predicting response. Our current effort is directed at selecting a group of such tests that can most practically be run on serum samples of cancer patients. Meanwhile, we are accumulating data, which, when subjected to computer analysis, will determine the usefulness of each such test for the proposed purpose and will select the best group of tests for increasing the probability of accurate predictions.

Three groups of patients are being studied, all of which have had documented malignant disease: (1) Patients clinically free of disease but with a high risk of recurrence, (2) patients with measurable or residual disease about to embark on a new treatment regimen, and (3) patients susceptible to the development of brain metastases. Groups 1 and 3 are being studied for recurrence of disease by measurements on serum and CSF, respectively. Group 2 is being studied for response to therapy.

NCI GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 16703

TITLE: Tumor-Associated Intestinal Cell Membrane Factors

PRINCIPAL INVESTIGATOR: Milton M. Weiser

INSTITUTION: Massachusetts General Hospital
Boston, MA

ABSTRACT: Determine the role of glycoprotein synthesis for the different surface membranes of the mature epithelial cells as well as attempt to clarify the intracellular source of these membrane glycoproteins. Characterize, purify, and analyze crypt cell surface glycoproteins and glycosyltransferases and compare them to villus cell surface membranes. Continue the study on the diagnostic and prognostic significance of the cancer-associated galactosyltransferase isoenzyme II. Study of the biological significance of this isoenzyme II by utilizing an animal model that has been established. The animal model will be used to test whether this isoenzyme II is important in establishing conditions favorable for tumor growth and metastases.

NCI GRANT PROJECT SUMMARY

AREA: Biochemical Markers

GRANT NO.: CA 14380

TITLE: Pancreatic Ductal Versus Duodenal Secretions

PRINCIPAL INVESTIGATOR: Thomas T. White

INSTITUTION: University of Washington
Seattle, WA

ABSTRACT: The primary purpose of this proposal is to describe the distinguishing characteristics of exocrine secretions obtained from patients with carcinoma of the pancreas compared with those found in chronic pancreatitis, as opposed to patients without disease. The significance of this investigation lies in the possibility that it may provide a single specimen electrophoretic test to distinguish patients with pancreatic diseases from those without disease. It is likely that the secretions of the pancreas are altered by these disease processes in a number of predictable ways which can be demonstrated by electrophoretic analysis, and which can be coupled with simple histological and chemical tests. There may be further, non-secretory proteins or enzymes in the pancreatic secretions arising from inflammatory exudates, breakdown of tumorous or other tissues into the ductal system. It is possible that some types of pancreatic carcinoma elaborate ectopic enzymes, isoenzymes, lysosomes, or trypsin-like enzymes which may account for the autoactivation of enzymes. The activation properties of secretion in patients with chronic pancreatitis and carcinoma may be related to ductal and/or acinar cellular involvement in the process, and will vary depending on the origin, as well as the degree, of differentiation of the tumor. Since intraductal activation occurs in at least some carcinomas of the pancreas, it may be possible to relate the activity of the juice to the type of tumor, the amount of inflammatory reaction seen, the degree of invasiveness of a given tumor, and to find isoenzymes responsible for these events. It is also probable that we may identify some of the substances in the 50% or more unidentified protein in the secretions from patients with carcinoma of the pancreas and chronic pancreatitis. While these studies will be primarily directed towards the development of a test on duodenal aspirates or endoscopically obtained secretions, it may be possible to later adapt our findings to the identification of specific substances in serum samples.

NCI GRANT PROJECT SUMMARY

AREA: Biophysical Methods

GRANT NO.: CA 19019

TITLE: Ultrasound Mammography

PRINCIPAL INVESTIGATOR: Gilbert Baum

INSTITUTION: Yeshiva University
New York, NY

ABSTRACT: The goal of this phase of the project is to (1) refine the ultrasonographic criteria so that non-palpable breast cancers can be detected, (2) reduce the volume of data that has to be recorded, read, and analyzed by improved methods of tumor localization; and (3) develop the algorithms for digital analysis of the acoustic texture of tissues. Optical and digital data compression, image enhancement, on-line signal processing, alternate display techniques, and the feasibility of computer sorting are to be explored to solve these problems. All B-mode ultrasonography and X-ray computerized axial tomography share these problems so that the solutions developed in this research program have universal application for cancer detection throughout the body.

An ultrasound mammography study we have already conducted has shown that palpable scirrhous carcinomas of the breast produce an acoustic area that contains weak echoes which are very absorbant.

The problem is locating the small volume of tissue characteristic of the tumor in the comparatively large volume of breast tissue and then proving that the chosen volume is the malignant tumor.

Serial scanned ultrasound mammography at 3.0 mm intervals produced by the new breast ultrasonoscope will be analyzed. This interpretation will be correlated with the pathological, clinical, surgical, and X-ray findings. The ultrasonograms will then be used to form three-dimensional ultrasonograms by optical holography and digitized for textural analysis.

NCI GRANT PROJECT SUMMARY

AREA: Biophysical Methods

GRANT NO.: CA 20423

TITLE: Studies on the Pathobiological Chemistry of Melanoma

PRINCIPAL INVESTIGATOR: Marsden S. Blois, Jr.

INSTITUTION: University of California
San Francisco, CA

ABSTRACT: The proposed research involves the identification of disease-correlated chromatographic peaks in melanoma urines; the development of a data-reduction system for the chromatograms; and the construction of a high-pressure chromatographic system for processing large numbers of samples.

NCI GRANT PROJECT SUMMARY

AREA: Biophysical Methods

GRANT NO.: CA 20631

TITLE: Magnetic Detection of Injury Current from Tumors

PRINCIPAL INVESTIGATOR: David Cohen

INSTITUTION: Massachusetts Institute of Technology
Cambridge, MA

ABSTRACT: There are reasonable grounds for believing that tumors may generate a steady ion current in the surrounding tissue and fluid. This current would consist of injury current and/or liquid-junction current. In principle, the detection of this steady current with surface (skin) electrodes could reveal the presence of the underlying tumor, in a non-invasive way. However, steady potentials originating in the skin will interfere with this detection, hence pose a practical difficulty. Recent measurements of the steady current generated by breast tumors, using surface electrodes, show some electrical activity from the tumors; there is large scatter supposedly due to the interfering skin potentials. It is proposed here to again measure the steady current generated by breast tumors, but the magnetic field produced by the current will be measured instead of the surface potential. The magnetic field is free of skin interference. Successful magnetic measurements of another form of injury current have already been made, due to injured canine hearts; this current was measured non-invasively around the intact canine torso. The work proposed here is a two-year pilot project, in which magnetic measurements will be made over the chests of ten normal men and ten normal women (as controls), then of ten breast-tumor patients. These measurements will be made in the MIT magnetically shielded room using a superconducting detector. Computer techniques will be used to aid in the analysis of the measured magnetic fields in order to localize the current sources. If magnetic detection of steady currents from tumors is found to be feasible, an assessment will be made of the clinical possibilities of this new technique.

NCI GRANT PROJECT SUMMARY

AREA: Biophysical Methods

GRANT NO.: CA 14988

TITLE: Altered NMR Signals of Water in the Cancer Cell

PRINCIPAL INVESTIGATOR: Raymond V. Damadian

INSTITUTION: Downstate Medical Center
New York, NY

ABSTRACT: The proposed research is directed at achieving deeper understanding of the basis for prolonged NMR relaxations from water in cancer tissue. Studies are planned for the determination of "fixed charge" composition, alkali cation content cellular potentials and water, all of which are known to be interdependent phenomena. Work will be carried out to detail the sequence of changes in the above properties as a cell goes through the process of malignant transformation in vitro. NMR will be used to monitor other nuclei of biological importance and to characterize the malignant change (e.g., K39, P31, N14). Finally, use will be made of pulse-gradient techniques to gain additional insight into the motional freedom of water molecules and the barriers to diffusion within the cancer cell.

NCI GRANT PROJECT SUMMARY

AREA: Biophysical Methods

GRANT NO.: CA 16466

TITLE: Polarography with Albumin and Cancerous Human Blood Sera

PRINCIPAL INVESTIGATOR: Izaak M. Kolthoff

INSTITUTION: University of Minnesota
Minneapolis, MN

ABSTRACT: On the basis of results obtained in voltammetry of bovine serum albumin (BSA) at the hanging mercury drop electrode (HMDE) it will be possible to account for many characteristics of "Brdicka currents" of albumin in the presence of cobalt salts at the dropping mercury electrode (DME). The occurrence of pronounced minima in these polarograms, the effect of drop time on the current during the growth of a drop, and the effect of the height of mercury on the Brdicka current may now be interpreted.

It is further proposed to study, in cooperation with Professor John Overend, the structure of BSA adsorbed as a monolayer on mercury and possibly on other metals. From cyclic voltammetry polarograms at the HMDE it has been concluded that on reduction of cobalt (II) to cobalt (0) in the presence of BSA an unstable compound, Co (0)....minus SXP is formed. It is proposed to study the stability and the properties of this compound and of those obtained with other disulfide-containing proteins. In addition, it will be investigated whether nickel, iron, and other metals form similar compounds.

A critical study is planned of the polarographic cancer test in deproteinated blood sera. Various methods of deproteination, including ultrafiltration, will be used. The effects of calcium ions and of tetraalkylammonium salts on the polarograms will be tested.

The physico-chemical, serological, and carcinogenic properties of completely reduced albumin, P(SH)35, will be studied. In addition, similar studies will be made with incompletely reduced albumin by various methods.

NCI GRANT SUMMARY PROJECT

AREA: Biophysical Methods

GRANT NO.: CA 18705

TITLE: Ocular Cancer Detection by Hematoporphyrin Fluorescence

PRINCIPAL INVESTIGATOR: David L. Krohn

INSTITUTION: New York University
New York, NY

ABSTRACT: An amelanotic malignant melanoma, indigenous to hamsters, has been grown in serial transplants in the rabbit eye (Greene tumor). We have been able to transplant this tumor with 90% successful takes in the subchoroidal space of rabbits. This was done without immunosuppression and with a technique similar to that used in the cyclodialysis procedure in ocular surgery. These tumor implants imitate in initial appearance classical choroidal tumors in man. They differ in a number of ways, including consistent lack of pigment and a speed of growth sufficient to cause the tumor to occupy most of the eye within four weeks of implantation. In the early phases, however, they can be clearly established as successful tumor takes by indirect ophthalmoscopy. The tumor at this time and in this location is a suitable experimental model for development of methods of positive identification of tumors, and for pathological studies of the effect of treatment methods such as cryodiathermy. The speed of growth of the tumor presents a stringent test of a treatment method. The report of the method of introduction of the tumor is shortly to be published. The proposal is for work in the two areas mentioned below: (1) Further development of a detection technique for posterior ocular melanomas with anhydrotetracycline fluorescence and differential filtration to neutralize the effect of lens fluorescence interference, using the experimental posterior melanoma, with histological control. (2) Cryogenic destruction of small established melanomas by transconjunctival application with histological studies at various intervals following treatment; development of treatment schedules for resistive or large lesions; exploration of use of transvitreal cryodiathermy under ophthalmoscopic control.

NCI GRANT PROJECT SUMMARY

AREA: Biophysical Methods

GRANT NO.: CA 17335

TITLE: Liquid Cholesterol Ester Thermography of the Breast

PRINCIPAL INVESTIGATOR: Stanley M. Rogoff

INSTITUTION: University of Rochester
Rochester, NY

ABSTRACT: Thermography has now been established as useful in the diagnosis of malignant neoplasms of the breast. The wide application of thermography of the breast, however, is limited by the lack of availability of the thermographic apparatus to many hospitals and clinics because of expense.

We are proposing that thermography of the breast with liquid cholesterol esters would have certain economic advantages which would allow much wider application of the thermographic diagnostic technique. Thermography with liquid crystals, until the present time, has not been accepted in part because of difficulties in removing the liquid crystals and the underlying necessary black base after the examination is over. It is proposed that the new technique of easily applied and removed black polymer substrate base and liquid crystals be tested for accuracy compared to standard infrared thermography with the thermographic apparatus. Patient acceptance and the question of the possibility of skin irritation from these chemicals will be investigated. Specifically, women undergoing breast biopsies in Rochester will be evaluated by standard thermographic and liquid crystal techniques. Molybdenum tube X-ray mammography will also be performed for comparison. Confirmation of diagnoses will be made by pathological examination.

NCI GRANT PROJECT SUMMARY

AREA: Biophysical Methods

GRANT NO.: CA 14335

TITLE: EPR Studies on Detection and Treatment of Cancer

PRINCIPAL INVESTIGATOR: John D. Zimbrick

INSTITUTION: University of Kansas
Lawrence, KS

ABSTRACT: It is proposed to continue a comprehensive research program designed to investigate the use of electron paramagnetic resonance (EPR) as a technique for the early detection of cancer, for monitoring the progress of cancer therapy and for elucidating the nature of the free radicals involved in cancer. Detailed EPR measurements of serum ceruloplasmin will be made on blood samples from women admitted to hospitals prior to breast biopsy and compared with appropriate control levels to determine whether this technique provides a statistically reliable marker for breast cancer. EPR measurements of serum ceruloplasmin will continue to be made on blood samples obtained from patients during the course of chemotherapy to determine the statistical reliability of the measurements as prognosticators of the success or failure of the therapy. A study, based on epidemiological principles, will be initiated on EPR measurements of ceruloplasmin levels in blood obtained from male smokers 40 years of age or greater, who have accumulated at least 40 pack-years of smoking history, to determine whether the technique provides a statistically reliable marker for lung cancer. A variety of EPR techniques such as spin-labeling, endor and spin-echo measurements will be applied to blood constituents to detect possible differences between the cancerous and non-cancerous state which may exist in these constituents.

NCI GRANT PROJECT SUMMARY

AREA: Bladder Cancer Task Force

GRANT NO.: CA 14135

TITLE: Immunology of Bladder Tumors

PRINCIPAL INVESTIGATOR: Warren H. Chapman

INSTITUTION: University of Washington
Seattle, WA

ABSTRACT: We want to continue these studies of immune reaction to tumor with three specific aims: (1) To study cell-mediated immune reactions to bladder tumor antigens and their blocking by serum in human patients with the emphasis on common tissue type specific antigens but also looking for unique antigens specific for each tumor and correlating this with the patient's clinical course. (2) To study, in parallel with the above, cell-mediated immunity and humoral factors to common tissue type specific antigens and unique antigens to animal bladder papillomas and carcinomas, and to correlate these with tumor behavior _in vivo._ (3) To develop in the animal immunologic methods of preventing the induction of bladder tumors and of treating established tumors.

Studies on the _in vivo_ correlation of the _in vitro_ immune responses in the human and in the animal model will be carried out in parallel. The animal models will then be used to develop methods of manipulating the immune response in order to increase tumor destruction _in vivo_.

We believe that these studies will assist in the prediction of prognosis in the bladder tumor patient and ultimately lead to the development of a rational program of immunotherapy to add to the present modalities of radiation, surgery and chemotherapy.

NCI GRANT PROJECT SUMMARY

AREA: Bladder Cancer Task Force

GRANT NO.: CA 16725

TITLE: Urine Cytology

PRINCIPAL INVESTIGATOR: George M. Farrow

INSTITUTION: Mayo Foundation
Rochester, MN

ABSTRACT: The objectives of this study are threefold: (1) To define the accuracy of urine cytology in the detection of bladder cancer with special emphasis on the relationship of cytologic findings to tumor characteristics such as histologic type, grade, size and stage and to compare cystoscopy as a diagnostic tool. (2) To refine technical factors in preparation of cytologic material. (3) To study the cytologic, pathologic and biologic evolution of early bladder cancer detected in a preclinical stage by cytology. The study utilizes a large outpatient population, predominantly urologic, in which routine cytology and cystoscopy examinations are performed and complete data on findings are recorded for computer retrieval and analysis. This cytologic screening has yielded 115 patients, without previous history of bladder tumor in whom positive cytologic findings for carcinoma have existed without cytoscopic evidence of neoplasm. Seventy-four of these patients have been subsequently proven to have in situ carcinoma of the bladder and the bladders of 34 of these submitted to total cystectomy have been totally mapped and studied pathologically by step sectioning. The remaining patients are being treated by a variety of modalities and are being closely followed.

NCI GRANT PROJECT SUMMARY

AREA: Bladder Cancer Task Force

GRANT NO.: CA 17444

TITLE: CHI to Bladder Cancer TAA *In Vivo* and *In Vitro*

PRINCIPAL INVESTIGATOR: Ariel C. Hollinshead

INSTITUTION: George Washington University
Washington, DC

ABSTRACT: We have purified and characterized tumor-associated antigens from transitional cell carcinoma of the bladder. We have developed antisera to the bladder cancer tumor-associated antigens, for a spectral analysis of the use of such antisera in *in vitro* assays for assessment of reactivity with material from patients with *in situ* carcinoma, hyperplasia and invasive carcinoma of the bladder as well as from normal individuals and from patients with other types of cancer. An extensive series of studies have been carried out to determine whether immunofluorescence, complement fixation or radioimmunoassay might be valuable. In addition, we have been assessing other *in vitro* assays, such as lymphocyte migration inhibition and cytotoxicity for reactivity with the separated antigens. We have found the immunofluorescence tests to be the most useful, using the antisera, and the lymphocyte migration inhibition to be the most useful using the TAA. We are conducting a coded series of skin tests using TAA and controls in bladder cancer patients at different stages in the development of the disease, with ancillary testing of patients with other types of cancer of similar age, sex and stage of disease.

NCI GRANT PROJECT SUMMARY

AREA: Bladder Cancer Task Force

GRANT NO.: CA 15803

TITLE: Automation of Bladder Cancer Cytology by TICAS

PRINCIPAL INVESTIGATOR: Leopold G. Koss

INSTITUTION: Montefiore Hospital and Medical Center
New York, NY

ABSTRACT: The purpose of this study is the computer analysis of digitized images of urothelial cells from the urinary sediment. The digitized images are obtained by scanning cells stained with Papanicolaou method by means of a Zeiss SMP scanning microscope at 0.5 m intervals, on line with PDP-12 (36K) computer. The cell images are forwarded on tape to the University of Chicago for analysis on dedicated PDP-10 computer wherein resides the taxonomic intracellular analytic system (TICAS) for cell analysis. In the initial stage of this project, a computer analysis of benign (neg) and malignant (pos) cells could be carried out with a high degree of accuracy (plus or minus 10%), by the use of both the supervised learning program distill and unsupervised learning algorithm pindex. The next step in this program has been computer classification of cells impossible to classify by visual means, hence atypical (aty). For each one of the 21 features tested, the values for aty cells were intermediate to the values of neg and pos cells. Using the pindex program, the aty cells could be split into subsets (neg, pos and aty) and allowed the construction of individual patient charts. The diagnostic and prognostic value of these charts is under continuing investigation and may lead to a computer assessment of diagnosis and prognosis of cancer and precancerous states of the urinary bladder.

NCI GRANT PROJECT SUMMARY

AREA: Bladder Cancer Task Force

GRANT NO.: CA 15553

TITLE: Tumor-Specific Immunity in Bladder Cancer

PRINCIPAL INVESTIGATOR: Shant Kumar

INSTITUTION: Victoria University of Manchester
Manchester, England

ABSTRACT: The object is to study the immunologic responses directed against tumor-specific antigens during the development of human bladder cancer. Workers in the dyestuffs industry exposed to the carcinogens alpha and beta naphthylamine before 1952 will be studied at regular intervals over a five-year period. It is anticipated that during this period, a significant number of new cases should arise in the population considered to be at "great risk." Lymphocytotoxicity, complement-mediated serum cytotoxicity, and blocking factor activity will be examined against a panel of allogeneic bladder cancers on each occasion. The results of these tests will be evaluated along with data obtained by regular examination of urine for red cells and, where appropriate, more detailed examination of the urinary tract including biopsy. It should be possible to determine the time relationships of the development of lymphocytotoxicity, serum antibody, blocking factor and overt tumor. It is possible that these studies may provide earlier diagnosis and an index of prognosis in carcinogen-induced bladder cancer.

NCI GRANT PROJECT SUMMARY

AREA: Bladder Cancer Task Force

GRANT NO.: CA 14137

TITLE: Bladder Cancer -- Meniscus Gradient and Matrix Culture

PRINCIPAL INVESTIGATOR: Joseph Leighton

INSTITUTION: Medical College of Pennsylvania
Philadelphia, PA

ABSTRACT: We are developing tissue culture model systems to elucidate the biologic characteristics of early abnormal proliferations in urothelium obtained from patients by transurethral resection. Specimens from over 70 patients have been cultured in a three-dimensional matrix of collagen-coated cellulose sponge and a variety of morphologic changes have been identified after one week of cultivation. To increase the breadth of our ability to subclassify lesions of similar histopathology, we have tried to cultivate clinical tumors in the meniscus-gradient model, where monolayers of bladder carcinoma cell lines have shown distinctive zonal responses to the gradient of decreasing oxygen tension. We are now combining collagen-coated cellulose sponge and meniscus gradient principles, and early work is very encouraging. As an additional tool for subclassification of clinical lesions we are developing a series of molecular probes using bladder cancer cell lines.

NCI GRANT PROJECT SUMMARY

AREA: Bladder Cancer Task Force

GRANT NO.: CA 17458

TITLE: Tumor-Specific Antigens in Human Bladder Cancer

PRINCIPAL INVESTIGATOR: Martin G. Lewis

INSTITUTION: McGill University
Montreal, Canada

ABSTRACT: Objectives: To investigate and identify the antigenic components in human bladder cancer and to attempt to classify these components into both tumor-specific and tumor-associated components.

Approach: Due to the restricted size of the tumor material, emphasis has been placed on the development of micro methods for the detection of serum antibodies directed against the various tumor antigens. The patient's response to both his own tumor and the tumor of the other bladder carcinomas is monitored by (1) immunofluorescence, (2) counter-current immunoelectrophoresis, and (3) enzyme-linked immunoadsorption test. All three of these systems will be used to show the different responses that occur when both the autologous and homologous sera are tested against both cytoplasmic and plasma membrane preparations of the tumor. The specificity of these reactions will be checked by both immune blocking and specific absorption experiments. The use of other unrelated tumors, e.g., melanoma, will help to establish the specificity of the reactions observed.

NCI GRANT PROJECT SUMMARY

AREA: Bladder Cancer Task Force

GRANT NO.: CA 14134

TITLE: Automation of Urinary Cytology for Cancer Detection

PRINCIPAL INVESTIGATOR: Myron R. Melamed

INSTITUTION: Memorial Hospital for Cancer and Allied Diseases
New York, NY

ABSTRACT: The purpose of this program is to develop instrumentation and techniques for automated cytology of exfoliated urinary bladder epithelium, to be used in early detection and diagnosis of bladder carcinoma. Additional goals are to use this instrument system with specially developed cytochemical procedures for measuring conformational changes in DNA and RNA _in situ_ to differentiate between cells of papillomas, low grade carcinomas and high grade carcinomas, and to quantitate irradiation and drug treatment effect by the same means.

The instrument system consists of a flow-through cytofluorometer which can be used to measure native and denatured DNA and RNA per cell within intact cells in suspension. It will be modified to also measure optical parameters for differentiating cells by fluorescent pulse shape and by coherent light scatter. Multiparameter measurements per cell at a rate of several hundred per second will be obtained on 5,000 cells per sample, then stored and analyzed by a dedicated mini-computer to characterize different kinds of cell populations by pattern recognition techniques. Work to date has shown that this approach with metachromatic fluorescent staining by acridine orange will discriminate between bladder epithelial cells and other cell types, with some overlapping. We have now developed new cytochemical techniques for measuring conformational changes in DNA and RNA _in situ_ that will distinguish cell types by qualitative as well as quantitative differences in DNA and RNA, with initially excellent results.

NCI GRANT PROJECT SUMMARY

AREA: Bladder Cancer Task Force

GRANT NO.: CA 20388

TITLE: Immunodiagnostic Assay of Bladder Carcinoma

PRINCIPAL INVESTIGATOR: Anthony P. Monaco

INSTITUTION:
New England Deaconess Hospital
Boston, MA

ABSTRACT: Studies have shown that a rabbit anti-bladder cancer urine can be produced and used in conjunction with various monospecific antisera for the detection of urine components related to bladder cancer. Regarding a urine positive when it reacted with two or more antibodies resulted in the diagnosis of 64% of the papilloma urines, 92% of the cancer urines vs. only a 7% false positive rate.

Also, in addition to these serum-related components, at least two tumor specific antigens (TSA) have been partially purified and characterized from cancer urine. An antiserum which reacts specifically with these TSA has been prepared and is currently being tested for its usefulness for the early diagnosis of bladder cancer.

NCI GRANT PROJECT SUMMARY

AREA: Bladder Cancer Task Force

GRANT NO.: CA 16769

TITLE: CEA in Urogenital Carcinomas

PRINCIPAL INVESTIGATOR: Eugene P. Ornellas

INSTITUTION: Massachusetts General Hospital
Boston, MA

ABSTRACT: CEA levels in the blood (b) and urine (u) of patients with genitourinary neoplasms (bladder, prostate and renal) will be determined prior to the use of diagnostic and therapeutic modalities, during their application and immediately afterwards as well as on a long-term basis. The CEA levels will be related to stage/grade/differentiation of the tumors, the diagnostic and therapeutic events which will occur, and to the existence of urinary and extraurinary factors that may change these levels. Determinations will be duplicated and related temporally to the factors mentioned above. From those studies a decision can be made as to relative value of determining CEAb and CEAu in different clinical settings. Very preliminary studies suggest the possibility that large increases or decreases in the levels of CEA in the urine following transurethral resection of the bladder may be related to the extent of tumor resection.

NCI GRANT PROJECT SUMMARY

AREA: Bladder Cancer Task Force

GRANT NO.: CA 16939

TITLE: Specific Antibodies to Bladder Carcinoma Tumor Antigen

PRINCIPAL INVESTIGATOR: Amadeo J. Pesce

INSTITUTION: University of Cincinnati
Cincinnati, OH

ABSTRACT: This work attempts to prepare antisera to a specific bladder carcinoma antigen(s) and then to isolate this antigen(s). The initial approach is to prepare antisera to bladder carcinomas, fetal bladder, normal adult bladder and control renal tissue. These antisera will be tested using immunohistologic techniques with both frozen and freeze substituted tissue. Positive sera will be absorbed with normal bladder and various other protein preparations, and control antigens. The absorbed antisera will be retested by the same immunohistologic techniques to establish if tumor specific antisera has been obtained. In later studies bladder carcinoma tissue will be extracted as described for the carcinoma embryonic antigen to establish if a similar or analogous antigen exists for these tumors.

NCI GRANT PROJECT SUMMARY

AREA: Bladder Cancer Task Force

GRANT NO.: CA 16969

TITLE: Human Urinary Bladder Tumor Antigens

PRINCIPAL INVESTIGATOR: David T. Purtilo

INSTITUTION: University of Massachusetts Medical School
Worcester, MA

ABSTRACT: Our objective is to identify bladder tumor-associated antigens (BTAA) in human urinary bladder cancer.

Heteroantisera are being raised in rabbits against BTAA prepared from hypotonic saline extracts, chromatographic antigenic fractions and whole carcinoma cells of fresh tumor or cultured bladder carcinoma cells. Following extensive absorption with lyophilized normal adult tissues, erythrocyte stroma and plasma, the specificity of the reaction of the antisera to bladder tumors is being tested using Ouchterlony immunodiffusion, immunoelectrophoresis, microcytotoxicity and immunofluorescent techniques. Cross reactivity of the BTAA antisera against various histologic types and grades of bladder carcinomas, extravesicular malignancies and embryonic antigens is being assessed using the appropriate above techniques.

Heteroantisera to normal bladder urothelium-specific antigens (BUSA) are also being raised against saline extracts and chromatographic fractions of normal human bladder urothelium. BTAA and BUSA are being quantified in tissues containing various bladder lesions using immunofluorescence. The results of these immunological studies will be correlated with the histopathologic appearance, stage and progression of the bladder tumors.

NCI GRANT PROJECT SUMMARY

AREA: Bladder Cancer Task Force

GRANT NO.: CA 14555

TITLE: Chromosomes of Human Bladder Tumors

PRINCIPAL INVESTIGATOR: Avery A. Sandberg

INSTITUTION: Roswell Park Memorial Institute
Buffalo, NY

ABSTRACT: The major aims of the project continue to be a correlation between (1) the chromosomal findings of early bladder lesions, particularly papillary tumors, with the cytologic picture and clinical course, and (2) the karyotypic picture in advanced carcinoma of the bladder with the response to therapy and clinical course, e.g., sensitivity to X-ray and/or chemotherapy, metabolic spread, recurrences, etc.

NCI GRANT PROJECT SUMMARY

AREA: Bladder Cancer Task Force

GRANT NO.: CA 15315

TITLE: The Control of Bladder Cancer

PRINCIPAL INVESTIGATOR: Walter Troll

INSTITUTION: New York University
New York, NY

ABSTRACT: The major objectives of the proposal are the development of rapid tests for urinary bladder carcinogens and the prevention of bladder cancer in man by use of protease inhibitors. The detection of bladder carcinogens will help environmental hazards in commercial dyes and the nature of the proximal carcinogens. Progress has been made in the understanding of mutations in microorganisms. The mutations appear to be due to error prone repair of DNA. This repair is induced when DNA is damaged and is incapable of supporting division. The induction is inhibited by protease inhibitors, and carcinogenesis is inhibited by protease inhibitors. The understanding of mutations in bacteria simplifies the measurement by using lambda phage lysis as indicator. We will apply this technique to urines of experimental animals fed dyes and other possible bladder carcinogens. We hope to apply this technique to urines of men possibly exposed to carcinogens as well. We will continue our work in preventing bladder cancer in Fisher rats fed (N-(4-(5-nitro-2-furyl)-2-thiazolyl formamide (FANFT) with protease inhibitors and cortical steroids, and N-butyl-(4-hydroxybutyl)-nitrosamine (BBN). This work will be carried out in cooperation with Dr. Joseph Leighton, Pennsylvania Medical College, and Dr. Leo Koss, Montefiore Hospital, New York.

NCI GRANT PROJECT SUMMARY

AREA: Cytology

GRANT NO.: CA 13271

TITLE: Automated Cancer Cell Diagnosis by the TICAS Method

PRINCIPAL INVESTIGATOR: George L. Wied

INSTITUTION: University of Chicago
Chicago, IL

ABSTRACT: The current project is the renewal application of the ongoing project to develop methods of computerized cancer cell diagnosis. The development of the project is to progress in interrelated areas: (1) improvement of the quality of cancer cell diagnosis, including the development of a computerized data bank of cancer cells and non-malignant cells, (2) simulation of clinical cell samples, including the development of performance testing criteria for prescreening devices for cancer diagnosis and synthesis of cell images, (3) evaluation of staining techniques and properties for computerized pattern recognition and cellular images, (4) assessment of the dynamics of the disease process as defined by the deformation of the covariance matrix of the image properties of scanned cells, (5) development of shape recognition algorithms, and (6) feasibility study on the usage of the TICAS method by other research teams. The system as proposed may also serve as the final stage of a fully automated cancer cell screening device, in which the system as proposed may also serve as the final stage of a fully automated cancer cell screening device, in which the TICAS method will take over the diagnostic assessment of an enriched sample or of a routine cytologic smear the alarm signals' coordinates of which were marked for refinding for the proposed automated diagnostic system.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 14854

TITLE: Studies on Cancer Cell Surface Glycoproteins

PRINCIPAL INVESTIGATOR: Howard J. Allen

INSTITUTION: Roswell Park Memorial Institute
Buffalo, NY

ABSTRACT: The overall objectives of this research project involve the isolation, chemical, structural and immunochemical characterization of tumor-derived glycoproteins at the cell surface and those elaborated into the culture medium which may play a role in cell-cell recognition phenomena and tumor antigenicity; and the elucidation of the mechanisms controlling modulation of glycoprotein expression. Emphasis will be given to murine ascites systems and human ovarian cancer.

Glycoproteins will be isolated primarily by affinity chromatographic techniques using insolubilized lectins. Metabolically labeled (with glycoprotein precursors) radioactive glycoproteins will be used to provide an assay system for tumor-derived glycoproteins.

Glycoproteins correlated with murine tumor attenuation as a result of *in vitro* growth will receive emphasis.

Changes in activities of glycosyltransferases associated with glycoprotein changes will be studied using tumor-derived glycoproteins as acceptors.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 12389

TITLE: Immunochemical Studies of Gastrointestinal Cancer

PRINCIPAL INVESTIGATOR: Elliot Alpert

INSTITUTION: Massachusetts General Hospital
Boston, MA

ABSTRACT: The overall objectives of the project are to identify and characterize carcinofetal antigens and proteins of the gastrointestinal tract. Work this coming year will be devoted to further studies of the antigenic determinants of carcinoembryonic antigen by haptene inhibition, and characterization of an unusual molecular form of serum carcinoembryonic antigen.

We intend to test a number of other synthetic glycopeptides, of known chemical structure, by haptene inhibition radioimmunoassay for CEA. We also intend to test several additional antisera to CEA for their ability to recognize the unique CEA antigenic determinants described above. We hope to further characterize this unique serum CEA-like material initially by Sephadex gel filtration, perchloric acid solubility and isoelectric point. If enough sera containing the CEA-like antigen can be obtained, we hope to perform further purification and chemical analysis of this CEA-like antigen.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 17687

TITLE: Wilms' Tumor Antigens

PRINCIPAL INVESTIGATOR: John W. Beierle

INSTITUTION: University of Southern California
Los Angeles, CA

ABSTRACT: The purpose of this investigation is to further examine an antigen(s) found associated with the Wilms' tumor (nephroblastoma). One antigen has been found by immunodiffusion to be cross reactive with fetuin, a glycoprotein found in fetal calf serum. This antigen has also been found in *in vitro* cultures of Wilms' tumor, the Witu cell line. It is our intent to determine if this antigen as isolated by chelation (EDTA) is related to an antigen reported to be Wilms' associated by other workers using phytic acid and fluorocarbon extraction procedures. We further wish to develop more sensitive methods, other than double-immunodiffusion, to detect the presence of the antigens in tumors, serum, and in tissue culture. These include radioimmunoassay and autoradiography of immunodiffusion plates. In addition, a microcytotoxicity assay will be attempted to determine if anti-fetuin serum can be cytotoxic to Wilms' tumor cells *in vitro*. Affinity column chromatography will also be utilized in an attempt to isolate the antigen in a more highly purified form for subsequent studies. Isoelectric focusing using ampholines in acrylamide gel and in Sephadex columns will be utilized for detailed analysis and finite purification of the Wilms' antigen as well as determining which cross-reactive antigenic determinants are present in fetuin subfractions. The goal of these studies is to develop a rapid and sensitive assay for detection of this antigen, leading to eventual study of its uniqueness to Wilms' tumor, or other tumors, or even as to its specificity to tumor tissue per se.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 15556

TITLE: Antigens and Immunity in Human Lung Cancer

PRINCIPAL INVESTIGATOR: C. Elliott Bell, Jr.

INSTITUTION: Washington University
University City, MO

ABSTRACT: Overall objectives of total project: To identify and characterize one of more important plasma membrane tumor-associated antigens (TAAs) in human lung cancer which are absent from late fetal and normal adult tissue and which are immunogenic in humans; to determine the occurrence of the TAA(s) in host plasma and sputum, and to determine the status of host cellular and humoral immunity to the TAA(s); to determine the relationships of the above parameters to the course of disease, to each other, and to therapy for the purpose of identifying parameters which can be measured to provide earlier and more accurate diagnosis, treatment, and assessment of prognosis.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 19905

TITLE: Characterization of Human Breast Cancer Glycoproteins

PRINCIPAL INVESTIGATOR: Dani P. Bolognesi

INSTITUTION: Duke University
Durham, NC

ABSTRACT: Information concerning human breast cancer specific surface antigens will be obtained through the isolation and characterization of glycoproteins from human breast cancer cells and breast cancer patients' body fluids. Purified proteins will be utilized to produce specific antisera which will be used to develop sensitive immunochemical and biological assays. Techniques will be devised for the detection and localization of these components in the tumor and circulating fluids of breast cancer patients. Information concerning a possible relationship of the purified proteins to surface glycoproteins of oncornaviruses will be obtained by specific viral glycoprotein assays. Attempts to induce human breast cancer cells to produce virus or virus proteins will be made utilizing hormones and DNA analogs.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 18362

TITLE: Immunodiagnosis of Cancer with Chorionic Gonadotropin

PRINCIPAL INVESTIGATOR: Glenn D. Braunstein

INSTITUTION: Cedars-Sinai Medical Center
Los Angeles, CA

ABSTRACT: The objectives of the proposed work are to increase the sensitivity of the beta subunit radioimmunoassay for human chorionic gonadotropin in order to further examine its usefulness as a biochemical marker for neoplasia, and to determine the specificity of human chorionic gonadotropin as a tumor-associated antigen in the non-pregnant state. The sensitivity of the method will be increased by adsorption of HCG from blood samples onto concanavalin A, elution and concentration, followed by measurement with an improved antiserum directed towards the beta subunit of HCG. The specificity of the assay will also be increased by the generation of new antisera to the native beta subunit, as well as modified forms of the beta subunit of HCG. Studies will also be carried out on the HCG-like glycoprotein present in the normal human testes, and further purification and characterization of this material will be accomplished. Finally, a prospective evaluation of the value of HCG measurements for the immunodiagnosis of cancer and for following the effects of therapy will be made by comparing patients whose tumors produce HCG or its subunits to those whose tumors do not, in regard to clinical presentation, duration of disease, duration and extent of disease, age, sex, race, tumor histology and grade, response to therapy, known areas of metastases, and survival.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 16932

TITLE: BAMP Tumor Antigen: Distribution and Immunochemistry

PRINCIPAL INVESTIGATOR: John E. Butler

INSTITUTION: University of Iowa
Iowa City, IA

ABSTRACT: This research proposes to study the immunochemistry and immunobiology of the BAMP-anti-BAMP antigen-antibody system and to evaluate its potential as a diagnostic tool for the early detection of cancer. The work will complete the chemical and immunochemical analyses of BAMP and the cross-reactive human protein we call HAMP. Meanwhile, the distribution of HAMP-positive biopsy material and anti-BAMP/HAMP positive sera in patients with various malignant and benign tumors, autoimmune disease, immunodeficiencies and other pathologies will be determined. Finally, the feasibility and practicality of developing a diagnostic test for cancer based on the BAMP-anti-BAMP system shall be explored.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 17089

TITLE: Early Diagnosis of Cancer and Cancer Metastases

PRINCIPAL INVESTIGATOR: Israel Davidsohn

INSTITUTION: Mount Sinai Hospital Medical Center of Chicago
Chicago, IL

ABSTRACT: With means available, cancer can be cured if diagnosed early, before cancer has spread too far. The early clinical findings require a biopsy for a diagnosis. The pathologist can (1) exclude cancer; (2) find changes, leaving no doubt as to the malignant nature -- the cancer may be then already invasive; (3) anaplasia may be moderate; or (4) cells with criteria of cancer may be close to normal cells (carcinoma *in situ*). It was established that some lesions of this type may be reversible. Treating such patients as having carcinoma may lead to unnecessary surgery. On the other hand, failure to be radical may deprive such patients of the benefits of surgery. The highly sensitive and specific red cell adherence (RCA) test detects the A, B and H antigens in tissues and permits one to diagnose some carcinomas earlier than any other method. The quantitative test which we developed increases the sensitivity of the adherence test. We will continue to test our results by studying prospectively and retrospectively a larger number of early and advanced cancers in different organs.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 16309

TITLE: Carcinofetal Human Isoferritins

PRINCIPAL INVESTIGATOR: James W. Drysdale

INSTITUTION: Tufts University
Boston, MA

ABSTRACT: This research is aimed at extending our investigations into the occurrence of human carcinoembryonic isoferritins and their possible value in serodiagnosis of cancer. Attempts will be made to determine whether an "abnormal" isoferritin we have found in human hepatoma and in early fetal livers is a true carcinoembryonic protein or occurs in non-malignant disease or normal adult tissues. Particular attention will be paid to isoferritins in placenta, ovarian carcinoma, and HeLa cells, tissues presently receiving intensive study in the cancer center in this university as models for phenotypic expression of carcinoembryonic proteins. Preliminary evidence indicates that all three tissues contain isoferritins corresponding to carcinofetal forms found in hepatoma. These isoferritins will be isolated from placenta and HeLa cells for detailed comparative structural analysis with normal tissue isoferritins. Attempts will be made to develop monospecific antibodies against the carcinoembryonic isoferritins in placenta for serodiagnostic purposes.

In related studies, investigations will be made into the occurrence of carcinoembryonic isoferritins in lines of HeLa cells characterized by their content of the Regan isozyme, a carcinoplacental form of alkaline phosphatase. Factors regulating the genetic expression and biosynthesis of the HeLa ferritins will be compared to those operating in normal cells. Attempts will be made to correlate the phenotypic expression of the carcinofetal ferritins with the cell genotype.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 14346

TITLE: Human Tumor-Associated Molecular Expressions

PRINCIPAL INVESTIGATOR: Thomas S. Edgington

INSTITUTION: Scripps Clinic and Research Foundation
La Jolla, CA

ABSTRACT: A distinctive event in neoplasia is the appearance of new, normally repressed, modified or conformation perturbed molecular species on the surface of tumor cells. These events present potentially new antigenic sites, neoantigens, by which cellular and humoral immunity may be invoked by the host and immunological surveillance mediated. Such neoantigens may be employed as discriminating markers for molecular and cellular events associated with neoplasia including gene derepression, oncogenic virus infection, and organizational changes of the cell surface that may reflect transformational events. Precisely defined tumor-associated neoantigenic markers also may be utilized in a pragmatic fashion for the diagnosis of neoplasia as well as in potential future immunotherapeutic approaches to cancer.

An as yet incompletely defined and established neoantigenic marker of neoplasia of the gastrointestinal tract of man is the so-called "carcinoembryonic antigen" (CEA). We propose to isolate in very highly purified form each of the six or more CEA molecular variants present in gastrointestinal tumors. Each apparent CEA variant will be characterized by quantitative primary binding immunoassays in respect to specificity and number of sites per molecule, and characteristic antigen-dependent binding affinity. These CEA molecules will be degraded to constituent polypeptide chains, fragments, and carbohydrate moieties to identify the CEA determinant(s) per se. Tumor association and significance in immunologic surveillance will be assessed by investigation of cell surface exposure, metabolic events regulating cell surface expressions, lymphocyte-mediated cytotoxicity and antibody-mediated cytotoxicity on tumor and normal colonic epithelial cells. These studies should provide the scientific basis upon which to base precise and discriminating investigations of the immunobiology of cancer in man.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 19336

TITLE: Isolation of Astrocytoma-Specific Antigens

PRINCIPAL INVESTIGATOR: Fred H. Hochberg

INSTITUTION: Massachusetts General Hospital
Boston, MA

ABSTRACT: The objective of the proposed research is the isolation of astrocytoma-specific antigens by means of the production of tumor-specific antisera in partially "tolerant" animals.

Research already done by the applicants indicates that antiserum to antigens present in biopsied astrocytomas may be produced by the immunization of rabbits made partially "tolerant" to normal human tissue (plasma and brain). Antisera produced in this fashion will be absorbed using insoluble immunoadsorbents until they no longer contain antibodies to normal human tissue as determined by counter-immunoelectrophoresis, hemagglutination, immunofluorescence, or cytotoxicity techniques. Using these absorbed antisera tumor tissue, sera, and spinal fluid from astrocytoma patients will be tested for the presence of astrocytoma-specific antigens by counter-immunoelectrophoresis, immunofluorescence and cytotoxicity methods. The tumor and organ specificities of any identified antigen(s) will be determined by testing the antisera against a panel of non-brain normal tissue and non-astrocytic malignant tissue. Using purified specific antisera, these astrocytoma-specific antigens will be isolated by immunoaffinity chromatography, ion-exchange and gel filtration column chromatography, and preparative gel electrophoresis.

Presently, the diagnosis of human astrocytomas is insensitive and expensive, and often requires invasive techniques. However, early diagnosis is important for improved patient prognosis. The isolation of astrocytoma-specific antigens will make possible the development of sensitive, inexpensive assays which will aid in diagnosis and treatment, and will thereby improve the prognosis of patients with these malignancies.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 19842

TITLE: Terminal Transferase and Surface Markers in Leukemia

PRINCIPAL INVESTIGATOR: Phillip C. Holland.

INSTITUTION: University of Kentucky
Lexington, KY

ABSTRACT: The specific aims of this proposal are to examine sequentially cell surface markers, surface ultrastructure and terminal deoxynucleotidyl transferase activity in blood and bone marrow lymphoid cells from children with acute lymphoblastic leukemia; to isolate and define subgroup populations of blood and bone marrow cells which contain terminal transferase employing cell separation studies; and to determine the relationship of these biochemical and biologic markers to disease activity, clinical course, prognosis and chemotherapeutic regimens. Terminal deoxynucleotidyl transferase is present normally only in high concentration in the thymus and in low concentration in the bone marrow. The enzyme has been found in the peripheral blood of acute lymphoblastic leukemia patients and in lymphoblastoid cell lines. Crude extracts of lymphoid cells from peripheral blood and bone marrow are assayed directly utilizing H3-DGTP as substrate and oligo D(PA)50 as initiator. The limit of sensitivity of the assay is 0.05 units per 10^8 cells. Spontaneous rosette formation with sheep erythrocytes will serve as a T cell marker. Rosette formation with complement-coated sheep erythrocytes and determination of surface bound immunoglobulins using fluorescein conjugated anti IgT, IgM and IgA will be utilized as B cell markers. Surface morphology will be characterized using scanning electron microscopy following critical point preparation. Serial observations of terminal transferase activity, cell surface markers, and surface morphology in a large group of patients with acute lymphoblastic leukemia may provide information which will have important implications for the classification, prognosis, and therapy of this disease.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 14294

TITLE: Tumor-Associated Changes of Intestinal Cells

PRINCIPAL INVESTIGATOR: Kurt J. Isselbacher

INSTITUTION: Massachusetts General Hospital
Boston, MA

ABSTRACT: We plan to continue to study tumor-related changes of intestinal epithelial cells with special emphasis on the changes in the structure, function and biosynthesis of cell membranes. These studies will involve comparisons of the membranes of undifferentiated crypt cells, mature villus cells as well as of fetal, adult and malignant intestinal cells. These studies will involve human intestinal cancer and that experimentally produced in animals.

Experiments will be carried out on changes in nutrient uptake and transport by malignant cells of the intestinal tract using both human and experimentally produced rat intestinal tumors. Transport will be studied using membrane vesicles derived from intestinal cell microvilli. These observations will be compared to studies in a more controlled tissue culture system using chick embryo cells.

Glycoprotein and glycolipid structure and biosynthesis will be studied in fetal, adult and malignant intestinal cells. Further investigations will be carried out to study human fetal-specific and human tumor concanavalin A reactive proteins such as galactosyltransferase. These will be compared to carcinoembryonic antigen (CEA). We hope to pursue studies on the value of and use of serum galactosyltransferase as an aid to the diagnosis of intestinal malignancy.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 08975

TITLE: Human Leukemia-Associated Antigens

PRINCIPAL INVESTIGATOR: Richard S. Metzgar

INSTITUTION: Duke University
Durham, NC

ABSTRACT: Human leukemia-associated antigens are detected by nonhuman primate antisera to leukemia cells from donors with different morphological classes of leukemia. In addition, antisera to RNA tumor viruses are studied for their reactivity with human leukemia cells. The antisera are tested by complement-dependent cytotoxicity and the specificity of the antisera established by absorption techniques.

The serologically defined simian antisera are then evaluated as diagnostic and nosology reagents and clinical management aids. In addition, the antisera are used to monitor the antigens in studies designed to isolate them and identify their molecular characteristics.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 16320

TITLE: Immunotherapy and Immunodiagnosis of Human Leukemia

PRINCIPAL INVESTIGATOR: Donald S. Miller

INSTITUTION: Duke University
Durham, NC

ABSTRACT: Leukemia-associated antigens (LAA) have been detected on circulating leukemic cells and immature leukocytes of patients having myeloproliferative disorders. In these studies serial examination of bone marrow cellularity, morphology and leukemia-associated antigen positive leukocytes will be performed during the treatment of acute non-lymphocytic leukemia. Comparison of peripheral blood and marrow findings will be made. Morphological data will be compared to serological results. The sensitivity of normal and leukemic populations at differing initial marrow cellularities will be assessed. Following chemotherapy the recovery rates of both populations will be determined. The effect of both cycle active and alkylating agent therapy will be examined.

Serial clinical and serological data on approximately 200 patients having leukemia or myeloproliferative disorders have been stored on computer tape. Programs are being prepared to analyze these data for prognostic indicators and important correlations.

A new immunotherapy trial for chronic granulocytic leukemia (CGL) has been initiated. Patients will be leukophoresed and their leukocytes frozen in liquid N_2. Peripheral blood remission will be induced and maintained by busulfan. Patients will be randomized to receive BCG and autologous leukemic cells or no immunotherapy. Sera from immunotherapy patients and controls will be examined for antibodies against LAA.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 15446

TITLE: Antigen-Antibody Interactions in Neoplastic Disease

PRINCIPAL INVESTIGATOR: Percy Minden

INSTITUTION: National Jewish Hospital and Research Center
Denver, CO

ABSTRACT: This project will continue its efforts towards development of a better understanding of the role of the immune response to microorganisms and its relationship to subsequent development of tumors. It proposes to prepare and characterize antigens from microorganisms and from human tumor cells and to perform primary binding types of tests with these components. Antigenic similarities between tumors and microorganisms have been found. It is possible that this type of sharing may be widespread and that "nonspecific" bacterial immunotherapy could be the outcome of shared or cross-reacting immunologic stimuli. The antigenic relationships between antigens and tumors in microorganisms will be investigated with respect to developing new and specific approaches to immunotherapy.

Immunoglobulins derived from guinea pigs and rabbits have anti-tumor activities against the line-10 guinea pig hepatocarcinoma. Antibodies may be a decisive factor in the development of resistance to this tumor. This will be studied with a view to developing rational methods of using antibodies to influence the pathogenesis of other tumors. Antibodies in normal and tumor bearer human sera were detected to a variety of bacterial, fungal and tumor-associated antigens. Sera from patients with leukemias and melanoma had a lower capacity to bind both microbial and tumor-associated antigen. Serial bleedings from patients with tumors will be studied to correlate changes in antibody levels and the presence of immune complexes with states of clinical disease. Information will be sought that can be of diagnostic and prognostic value.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 15641

TITLE: Computer Analysis of Lymphocytes from Leukemic Mice

PRINCIPAL INVESTIGATOR: George B. Olson

INSTITUTION: University of Arizona
Tucson, AZ

ABSTRACT: Lymphocytes which are responsible for cell-mediated immune and humoral responses can be divided into subpopulations on the basis of surface antigens and functional tests, but cannot be differentiated by ordinary light microscopy. This study, based upon computer analysis of objective image descriptors, will differentiate peripheral and thoracic duct lymphocytes from normal mice and mice infected with various types of murine leukemia viruses. Objective image descriptor values which differentiate subpopulations of T and B cells, subsets of T cells, activated and non-activated lymphocytes, leukemic and normal lymphocytes, and lymphocytes responding to a leukemic process will be ascertained. Such objective image descriptors will provide for the establishment of a limited data bank to differentiate lymphocytes, which cannot be differentiated by ordinary light microscopy, into subpopulations and subsets, to compare feature vectors of stimulated lymphocytes to feature vectors of lymphocytes functioning actively in immunosurveillance, and perhaps to detect feature descriptors of the leukemic cell before other signs of the leukemic process are evident.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 16071

TITLE: Soluble HL-A Antigens in the Sera of Cancer Patients

PRINCIPAL INVESTIGATOR: Michele A. Pellegrino

INSTITUTION: Scripps Clinic and Research Foundation
La Jolla, CA

ABSTRACT: The major effort will be to extend the biological and chemical characterization of HL-A alloantigens and to evaluate HL-A antigens in the sera of cancer patients to establish any variation in their qualitative and quantitative distribution. Attempts will be continued to correlate the expression of HL-A antigens with other cell surface markers or in vitro cell activities. To this end sufficiently pure HL-A antigens will be isolated from serum to permit their extensive molecular characterization, including amino acid sequence analysis. Efforts will be made to utilize HL-A xenoantibodies (produced in our laboratory by injection of purified HL-A antigens in rabbits and goats) to develop a sensitive radioimmunoassay to detect HL-A antigens in serum.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 20543

TITLE: Antigen-Antibody Complexes in Cancer Patients' Sera

PRINCIPAL INVESTIGATOR: Roger D. Rossen

INSTITUTION: Baylor College of Medicine
Houston, TX

ABSTRACT: Application of a sensitive test (the clq binding method) for the detection of soluble antigen-antibody complexes to sera from patients with a variety of tumors has shown that over 80% of 134 patients with cancer probably had circulating immune complexes. The quantity of these was inversely proportional to the duration of the disease and patients who had had cancer less than 5 months and who had evident disease remaining after surgery had the highest levels. Moreover, in following these patients for up to 7 months we have found that patients with high levels of clq binding activity (greater than 10%) tend to have a significantly higher rate of progression on therapy than do patients with lower clq binding activities. Thus, measurement of circulating immune complexes in sera may provide an estimate of residual tumor mass in a variety of tumors for which specific immunodiagnostic reagents such as carcinoembryonic antigen and its antibody are not available. Moreover, measurement of soluble complexes provides a means to identify sera rich in both tumor antigen and antibody so that these may be isolated, fractionated and purified. It is proposed that serial measurements of soluble complexes be studied in a wide variety of malignant diseases over a 5-year period to determine the value of the method in predicting both remission and progression of disease. It is also proposed that the complexes be used as a raw material for characterization and purification of tumor antigens to create new reagents for diagnostic purposes and also to investigate the physiological role of these complexes in the tumor-host interaction.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 12646

TITLE: Abnormal Metabolism of Cancer Patients

PRINCIPAL INVESTIGATOR: Daniel Rudman

INSTITUTION: Emory University
Atlanta, GA

ABSTRACT: This project is concerned with the isolation and characterization of cancer-related proteins which are excreted in the urine by patients with advanced cancer. For each purified protein, a specific radioimmunoassay (RIA) is developed. The usefulness of each new RIA in the diagnosis of neoplastic disease is then studied.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 20364

TITLE: Immunodiagnosis of Melanoma

PRINCIPAL INVESTIGATOR: Hilliard F. Seigler

INSTITUTION: Duke University
Durham, NC

ABSTRACT: The detection of melanoma-associated antigens in patient sera could serve as a valuable means of detection and diagnosis of the disease. Our primary objective is to develop a radioimmunoassay to detect these antigens. The project will require isolation of tumor antigens for use as a standard test system. Proteolytic digestion of tumor cells followed by chromatographic and electrophoretic procedures will be used to isolate the antigens. A chimpanzee anti-human melanoma antiserum has been produced and characterized. This reagent will be utilized in antigen isolation and for radioimmunoassay. Purified tumor antigen will be used to immunize rabbits. Melanoma patient and control sera will be studied in an effort to demonstrate the specificity and sensitivity of the radioimmunoassay. The assay is potentially valuable for early detection of new or recurrent disease. In addition, the study may provide valuable insight into the in vivo role of blocking factors. Serological diagnosis of solid tumors will also be performed. Further study of melanoma-associated antigens will be attempted, in particular, the possible association of known oncornavirus antigens with human and murine melanomas will be examined. In vivo localization of antibody to tumor is prerequisite for successful serotherapy. We will study in vivo localization of the chimpanzee anti-human melanoma antibodies in nude mice bearing transplanted human melanomas. In addition, the B16 murine melanoma of C57Bl/6 mice and rabbit anti-B16 antibody will be used as a model for in vivo localization.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 19304

TITLE: Human Leukemia and Lymphoma Associated Antigens

PRINCIPAL INVESTIGATOR: Byeong-Kuk Seon

INSTITUTION: Roswell Park Memorial Institute
Buffalo, NY

ABSTRACT: The primary objective is to identify cell surface materials which are associated with human malignant lymphoproliferative disorders and to isolate these materials in large quantities so that their chemical structures, such as amino acid sequence, can be determined and so that they can be used to induce immune response. Cultured as well as noncultured human malignant cells will be used to isolate the leukemia-lymphoma associated antigens (LLAA). We have recently detected antigen(s) common to several cultured human malignant T cell lines by the use of a sensitive radioimmunoassay involving ^{125}I-labeled antibody to human malignant T cells (MOLT 4). All of these cell lines were derived from the lymphocytes of patients with leukemia.

The use of cultured cells will allow us to isolate the LLAA in large quantities and further allow us to feed the cell with a complete complement of ^{14}C-amino acids so that we can isolate uniformly radiolabeled LLAA. The radiolabel marker on LLAA will greatly facilitate the chemical characterization, especially the amino acid sequence determination of LLAA. We will further attempt to isolate peptides which retain the tumor antigenicity, from the various digests of the uniformly ^{14}C-labeled and isolated LLAA. In another experiment, we radioiodinated MOLT 4 cells by the use of lactoperoxidase-catalyzed iodination and we are currently working on isolating the radioiodinated LLAA.

In the present ongoing project, we are detecting LLAA on cells by the combined use of the conventional complement-dependent cytotoxicity test and a sensitive radioimmunoassay. The use of the latter method may allow us to detect certain LLAA which will not be detected by the conventional cytotoxic method. As the antisera, we have prepared baboon and rabbit antisera to noncultured lymphocytes from patients with acute lymphoblastic leukemia and lymphosarcoma cell leukemia.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 18945

TITLE: Plasminogen Activators of Malignancy

PRINCIPAL INVESTIGATOR: Samuel C. Silverstein

INSTITUTION: Rockefeller University
New York, NY

ABSTRACT: Inhibitory antibodies directed against the plasminogen activator produced by a line of SV40 virus transformed hamster cells distinguish between plasminogen activators produced by different hamster tissues. These antibodies do not inhibit plasminogen activation by plasminogen activators from several lines of hamster cells transformed by other agents, demonstrating that immunologically distinguishable forms (isozymes) of plasminogen activators are produced by transformed cells from the same species. The research proposed in this application will (1) define the number of immunologically distinguishable forms (isozymes) of plasminogen activators produced by normal hamster tissues; (2) determine whether the transforming agent, the tissue of origin, or other factors are responsible for the production of specific isozymes by malignantly transformed hamster cells; and (3) evaluate the possibility that antibodies directed against isozymes of plasminogen activators may allow us to detect alterations in the levels of these enzymes in the sera of tumor-bearing animals.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 18578

TITLE: Secretory Component in Neoplasia

PRINCIPAL INVESTIGATOR: Mary A. South

INSTITUTION: Children's Hospital of Philadelphia
Philadelphia, PA

ABSTRACT: Secretory component (SC), ordinarily associated with SLGA in secretions onto mucous surfaces, has been found by immunofluorescence microscopy in human mammary carcinoma cells. This project will attempt to fully define the human tumor-SC system, and will extend the studies into an animal model.

Various types of tumors will be examined for the presence of SC. Already SC has been found in colon, bronchogenic, and bladder carcinomas. It seems reasonable to anticipate finding SC in all neoplasms of glandular epithelium, both primary and metastatic. Experiments will be done to prove that the SC is actually being produced by the tumor cells, and not passively adsorbed by them. Sera from patients with tumors will be examined for the presence of free SC, SLGA, and precipitating antibodies to SC. The tumor SC antigenicity will be compared to that of normal SC found in external secretions.

The well-established mouse mammary tumor system will also be examined for the presence of SC in tumor cells. If found, the same procedure as proposed for the human studies will be used to prove that SC is being produced by the tumor cells themselves. Then anti-mouse SC administration will be employed in an attempt to manipulate tumor growth and animal survival rates.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 19083

TITLE: Human Breast Cancer-Associated Antigens and Cytotoxin

PRINCIPAL INVESTIGATOR: Georg F. Springer

INSTITUTION: Evanston Hospital
Evanston, IL

ABSTRACT: We shall elucidate the nature of the human breast cancer-associated T antigen we have found. We will assess the interaction of it and related structures with the humoral (including complement) and cellular immunological defense mechanisms of the host. We will develop a "two-site" immunoradiometric assay and quantitate T antigen (which occurs neither in non-cancerous persons nor in fetuses) in serum since we have shown indirectly the presence of T antigen in the sera of carcinomatous patients. Specimens from patients and controls will be collected fresh under sterile conditions. Anti-T titer score and Ig values of the sera will also be determined. Human mammary gland suspensions of both malignant and benign specimens will be made, extracted and membranes isolated and purified. The biological activities of the solubilized membranes will be assessed and their physical, chemical, and immunochemical properties determined. We will employ glycoprotein and glycolipid isolation and characterization procedures where indicated. We will prepare T antigen from human blood group O erythrocytes and employ this antigen in vitro and in vivo like the cancer cell membrane antigens. Cellular immunity in direct and indirect (MIF) blood leukocyte migration inhibition methods will be determined in Agarose plates. The lymphoblastogenic response will be determined by stimulation of protein synthesis (^{3}H-leucine incorporation). Skin tests determining the afferent and efferent limbs of the sensitivity response will be done with common antigens, T antigen and DNCB. We will evaluate "specific" (autologous breast cancer preparations and T antigen) combined and not combined with "unspecific" (BCG) immunotherapy on the course and prognosis of patients with stage II and III breast carcinoma who had standard surgical therapy. An adjunct will be Akleran coupled to autologous anti-T (all humans possess anti-T), which permits "target"-oriented therapy. Human studies will include cancer patients given (1) immunotherapy alone, (2) immunotherapy plus chemotherapy, and (3) a control group.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 16434

TITLE: Core Grant: Tumor Immunology and Chemistry

PRINCIPAL INVESTIGATOR: Charles W. Todd

INSTITUTION: City of Hope Medical Center
Duarte, CA

ABSTRACT: The broad objective is to facilitate the immunologic control of cancer by providing information on tumor-associated antigens. Specific aims are: (1) To elucidate the structures and antigenic roles of the carbohydrate and protein portions of CEA. (2) To isolate CEA-like materials from the tissues of both malignant and nonmalignant diseases in which elevated CEA levels have been reported in the serum. (3) To examine the CEA-like materials isolated to see if they are chemically identical to the material isolated from colonic adenocarcinoma. If they are different, attempts will be made to identify the chemical nature of the differences. (4) To assist other research groups in research on CEA and other tumor antigens through provisions of reagents and in training personnel in radioimmunoassay techniques. (5) To search for new tumor antigens which may be susceptible to isolation and purification for structural studies. (6) To develop and apply techniques other than radioimmunoassay which may be helpful in establishing the role of the antigen in the evolution of the malignancy and may point the way to its application in the control of cancer. (7) To explore and develop techniques, such as mass spectrometry, which will enable structural information to be obtained on very small amounts of complicated materials. (8) To apply these and other techniques to structural studies of new tumor antigens as they become available.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 19538

TITLE: Thymic Activity in Plasma with Thymus Disorders

PRINCIPAL INVESTIGATOR: Jeremiah J. Twomey

INSTITUTION:
Baylor College of Medicine
Houston, TX

ABSTRACT: One of more biologically active peptides made by thymic tissues induces T cell markers and functions in some lymphocytes. The thymus, presumably through these products, plays a major role in the normal maturation of the T lymphocyte series and, at least in experimental animals, also contributes to sustaining the T lymphocyte series.

This laboratory has recently developed a bioassay that measures Thy 1.2 antigen induction on precursor cells from spleens of nude mice that are genetically programmed to express this thymus-dependent antigen. This simple and reproducible bioassay is applicable to testing thymic activity (as it applies to T lymphocyte induction) in human plasma. In this project, we wish to apply this new technique to the study of patients with thymomas and other thymic disorders.

Baylor University is a referral center for patients with myasthenia gravis; at present over 100 patients that attend this clinic are available for study. We wish to correlate thymic activity in the plasma of individual patients with disease severity, thymic histology (if thymectomy is performed) and clinical benefit from thymectomy.

Thymoma is a likely diagnosis in patients with anterior mediastinal masses. We wish to see if plasma thymic bioassay results prove diagnostically useful and, in particular, if neoplastic and benign thymomas can be distinguished from one another.

Sternberg described an acute childhood leukemia that appears to directly involve the thymus -- analogous to leukemia in AKR mice. We propose to study such children.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 17533

TITLE: Myelogenous Leukemia-Associated Antigens

PRINCIPAL INVESTIGATOR: Carl J. Wust

INSTITUTION: University of Tennessee
Knoxville, TN

ABSTRACT: We have developed and characterized a unique cell line (K-562) originally derived from a patient with chronic myelogenous leukemia (CML). This CML cell line has the Philadelphia (PHI) chromosome and is free of Epstein-Barr virus genome, Herpes-like virus and mycoplasm and does not have T or B cell markers. Such a cell line, which also can yield sublines with two and three PHI chromosomes, not only provides a controlled and reliable source of CML cells free of some common oncogenic viruses, but can also be examined for relative synthesis of specific antigen with respect to the karyotype.

These CML cells when injected into rabbits cause the production of specific antibody which demonstrates complement-dependent cytotoxicity for CML cells. In preliminary experiments, the cytotoxicity for CML cells is not removed if the serum is absorbed with either leukocytes or granulocytes from normal donors. Absorption with CML cells does effectively remove the cytotoxic activity. Furthermore, the immune serum is not cytotoxic for normal human leukocytes. Other data indicate that the antiserum is cytotoxic for leukocytes from patients with CML obtained prior to treatment or during relapse.

The purposes of this project are: (1) to evaluate the specificity of the antiserum and its use as a diagnostic and/or prognostic aid; (2) to isolate and characterize the CML specific antigen(s); (3) to characterize the antibody during the immune response at selected intervals and assess the cytotoxicity on cells from normal and human patients suffering from leukemias, lymphomas and several other hematologic and non-hematologic diseases.

NCI GRANT PROJECT SUMMARY

AREA: Immunology

GRANT NO.: CA 04486

TITLE: Pathology of the Digestive Tract Mucous Membrane

PRINCIPAL INVESTIGATOR: Norman Zamcheck

INSTITUTION: Boston City Hospital
Boston, MA

ABSTRACT: We are continuing the study of the immunopathogenesis of human digestive tract cancer by conducting integrated clinical, pathological and immunochemical studies. We will study (1) the pathophysiology and metabolism of CEA, essential for basic understanding of the clinical application of CEA (and of other tumor markers) in benign and malignant clinical states; (2) the role of the liver in the metabolism and excretion of CEA. CEA and other antigens produced by primary sites as well as by metastases to the liver are detectable in the secretions of liver, biliary tract, pancreas and duodenal juice. We will continue to identify and characterize immunochemically CEA, CEA-like and other tumor-associated substances in these fluids, compare them with primary and metastatic tumor sources, and to develop assays for use in assessing their clinical use. (3) Malignant ascites and pleural effusions provide large volumes of autologous human cancer cells growing in vivo and producing high concentrations of CEA, alpha-fetoprotein, and other macromolecules characteristic of malignancy. We will compare extravascular sources of CEA and other tumor markers with the primary tissue source, characterize them immunochemically, develop assays for them: (a) as a means for improving the detection of malignancy in effusions, (b) for identifying the primary tissue source, and (c) to evaluate their use in monitoring therapy. (4) We will utilize the fluids as a source for new tumor markers, and (5) elucidate the mechanisms of the formation of malignant effusions.

NCI GRANT PROJECT SUMMARY

AREA: Large Bowel Cancer Task Force

GRANT NO.: CA 17776

TITLE: Colonic Cancer in Ulcerative Colitis

PRINCIPAL INVESTIGATOR: William O. Dobbins, III

INSTITUTION: George Washington University
Washington, DC

ABSTRACT: This project is for an investigation of the role of periodic clinical, roentgenologic, sigmoidoscopic in colonoscopic biopsy and cytologic collections, and plasma and colonic CEA as to their predictive value in the detection of colonic carcinoma and ulcerative colitis. It employs a skilled team consisting of gastrointestinal clinicians, a pathologist, a radiologist, gastrointestinal morphologist, a gastroenterologist skilled in radioimmune assay, and a cytologist. New features of this project include (1) the addition of colonoscopic observations, biopsy collection, and cytology collection; (2) electron microscopic studies to more accurately define stages of differentiation of precancer; (3) correlation of serial serum and colonic CEA determinations with the above observation; and (4) organ culture and electron microscopic studies to further search for etiologic clues in ulcerative colitis.

NCI GRANT PROJECT SUMMARY

AREA: Large Bowel Cancer Task Force

GRANT NO.: CA 17491

TITLE: Characterization of Gastrointestinal Glycoproteins

PRINCIPAL INVESTIGATOR: Marianne L. Egan

INSTITUTION: City of Hope Medical Center
Duarte, CA

ABSTRACT: The broad objective is to isolate glycoproteins secreted by the gastrointestinal tract in normal, premalignant and malignant states. These glycoproteins will be characterized immunochemically and chemically. Knowledge of the structure of the glycoproteins secreted in these states will aid our understanding of basic biosynthetic changes in malignant transformation. Specific aims are (1) to isolate the substances found in gastrointestinal washings of normal individuals which inhibit in the radioimmune assay for carcinoembryonic antigen, CEA; (2) to isolate the substances found in gastrointestinal washings of subjects with premalignant disease states, such as ulcerative colitis, familial polyposis, and alcoholic cirrhosis, which inhibit in the radioimmune assay for CEA; (3) to characterize these substances chemically and immunochemically and to determine whether they are CEA, a degradation product of CEA, or a counterpart whose synthesis is altered by the malignant transformation; and (4) to apply this knowledge to develop improved diagnostic tests for cancer of the digestive system.

NCI GRANT PROJECT SUMMARY

AREA: Large Bowel Cancer Task Force

GRANT NO.: CA 15799

TITLE: A Model for Colonic Cancer-Associated Antigens

PRINCIPAL INVESTIGATOR: David M. Goldenberg

INSTITUTION: University of Kentucky
Lexington, KY

ABSTRACT: The overall objective of this project is the identification and characterization of tumor-associated antigens of human colonic tumors. Initially, this will be investigated by using human colonic cancer xenografts established in unconditioned golden hamsters and being continuously propagated in these hosts for the last 9 1/2 years. Methods to be employed in the purification of these antigens will include gel filtration, electrophoresis, ultracentrifugation, affinity chromatography, etc., and the development, where appropriate, of sensitive radioimmunoassays for specific antigens. Of immediate interest is the carcinoembryonic antigen (CEA) originally described by Gold and Freedman and synthesized by our human colonic cancer transplants. Immunological and chemical characterization of CEA purified from these tumors will be undertaken and the findings compared to similar preparations made from tumor specimens obtained directly from human sources. In addition to this work with CEA, the presence of other antigenic substances in these tumors will be explored with a view toward identifying colon-associated or colon-specific, normal or neoplastic markers. The relationship of these antigenic markers of colonic cancer to CEA will be elucidated by immunochemical and immunocytochemical methods.

NCI GRANT PROJECT SUMMARY

AREA: Large Bowel Cancer Task Force

GRANT NO.: CA 18620

TITLE: Studies of a New Colonic Cancer Marker (ZGM)

PRINCIPAL INVESTIGATOR: Leonard S. Gottlieb

INSTITUTION: Boston City Hospital
Boston, MA

ABSTRACT: More specific markers for colon cancer, in addition to CEA, are needed. Before extensive clinical trials are run on newly discovered markers, it is essential to define their cellular and subcellular localization to assure their validity as tumor markers.

This laboratory has recently detected a new tumor marker in both primary and metastatic colon cancer using zinc glycinate extraction procedures, and antibodies produced in tolerant rabbits. This marker (ZGM) was found in addition to CEA, was immunochemically different from CEA, was not detectable in normal colonic mucosa; and anti-ZGM activity was not removed by absorption with liver, spleen, plasma, colonic mucosa, purified CEA and blood group substances (A, B, H, Le_a and Le_b).

We propose to define the histological localization of ZGM in colo-rectal carcinoma utilizing immunofluorescent and immunohistochemical techniques, and to compare it with that of CEA. This will be done on tissues carefully dissected and histologically characterized. We will assess the specificity of ZGM for colo-rectal and other carcinomas, and for premalignant lesions such as colonic polyps. Tissue levels of ZGM will be correlated with prognostic histopathological parameters, such as tumor differentiation, invasiveness and lymphocyte and plasma cell infiltration.

NCI GRANT PROJECT SUMMARY

AREA: Large Bowel Cancer Task Force

GRANT NO.: CA 22370

TITLE: Antigenic Stimulus in Human Colon Carcinoma Immunity

PRINCIPAL INVESTIGATOR: Barry D. Kahan

INSTITUTION: University of Texas Health Science Center
Houston, TX

ABSTRACT: In spite of multiple modes of treatment, colon cancer remains a most common malignant disease in this country. The present investigations seek to biologically and chemically characterize cell surface antigens, not only distinctive of this malignancy, but also capable of eliciting immune, destructive responses in man. Using morphological, chemical, virological, and chemical tools, the applicant and his colleagues have described characteristic surface membrane differences between malignant and normal colon cells. Three surface membrane components of approximate molecular weights 45,000, 58,000 and 60,000 appear to be distinctive of the malignant state. Employing a two-dimensional electrophoretic analysis with a first dimensional separation by charge (isoelectric focusing), and a second dimension by molecular weight, the distinctive components have been isolated for precise chemical characterization. Adequate amounts of material are available from the applicant's own colon cancer cell strains, which have been demonstrated to contain pure colon epithelial cells by morphology, mucin production, desmosomes, specific markers (CEA, T antigen, CSA), and to represent malignant elements by unlimited growth, lack of contact inhibition, morphology, karyology, cloning on monolayers, and outgrowth in conditioned xenogeneic hosts. The distinctive proteins were shown to bind rabbit heteroantisera capable of killing only malignant, and not normal cells. The proposed investigations not only intend to precisely characterize the chemical nature of the distinctive proteins, but also to determine whether patients afflicted with colon cancer develop immune reactions toward them in the course of their disease, by the capacity of soluble materials to trigger blastogenesis and/or to inhibit lymphocyte-mediated cytotoxicity toward colon cancer cells. Since failure to respond to the distinctive proteins may indeed play a role in the progression of the disease, spleen cells from normal individuals will be immunized in vitro with tumor cells and then tested for their interactions with the soluble antigens. These studies may thus provide insight into the development of immunodiagnostic tools or immunotherapeutic treatment modalities to improve the survival of patients with this cancer.

NCI GRANT PROJECT SUMMARY

AREA: Large Bowel Cancer Task Force

GRANT NO.: CA 18466

TITLE: Tumor Markers in Human Ascites

PRINCIPAL INVESTIGATOR: Herbert Z. Kupchik

INSTITUTION: Boston City Hospital
Boston, MA

ABSTRACT: Current methods of analyzing human ascites do not always distinguish cancer from benign diseases. Studies were undertaken to assess the feasibility of measuring CEA activity in these fluids by a modified zirconylphosphate gel (Z-gel) radioimmunoassay as an aid to detection of colo-rectal cancer. These studies suggest that CEA or CEA-like material is present in malignant effusions and may be differentiated from non-CEA-like material in benign fluids by quantitative and/or qualitative evaluation in the radioimmunoassay. Assay of CEA activity in effusions may be an adjunct to cytology in the detection of colo-rectal cancer.

We are expanding our studies to (1) evaluate the range of values found; (2) correlate tumor morphology and CEA levels; (3) study the relationship between CEA activity and protein components in the fluids, and (4) immunochemically characterize the CEA-active material(s) and compare it with purified CEA prepared from colonic malignancies.

NCI GRANT PROJECT SUMMARY

AREA: Large Bowel Cancer Task Force

GRANT NO.: CA 16766

TITLE: Biochemical Markers in Diseases of the Large Bowel

PRINCIPAL INVESTIGATOR: Lee R. Morgan

INSTITUTION: Louisiana State University
New Orleans, LA

ABSTRACT: The purpose of this study is to identify possible biochemical markers in patients with cancer of the large bowel, chronic ulcerative colitis and other premalignant colon lesions. The parameters studied will be arysulfatases A and B, lactic acid dehydrogenase (LDH), and dihydrofolate reductase (DHFR), alkaline phosphatase, DNA, and carcinoembryonic antigen (CEA).

Colonic washings, colo-rectal tissue biopsies, 24-hour urine collections and blood from normal subjects and patients diagnosed to have colo-rectal carcinoma, ulcerative colitis, familial polyposis, and other premalignant colon lesions will be assayed for the above biochemical parameters.

Preliminary data from our laboratory suggest that there are increases in the arylsulfatases and alkaline phosphatase activities in colonic washings from patients with large bowel cancer as compared to normal controls. The CEA values in the colonic washings from patients that were normal controls, with CUC and with large bowel cancer. Arylsulfatase A appears to be more useful than the B isoenzyme and correlates better with the disease process.

We have automated the arylsulfatase A and B assays and plan to develop rapid assays for these enzymes that might allow their use for random urine specimens. No correlation between the enzyme activities or CEA values for colonic washings and urine or plasma in the same patient were noted. The values obtained for the latter two fluids appeared to reflect the stage of the disease process.

The usefulness of serum, urine and colonic CEA and hydrolytic enzymes in the management of ulcerative colitis and predicting early malignant changes in the large bowel is the overall goal of this project.

NCI GRANT PROJECT SUMMARY

AREA: Large Bowel Cancer Task Force

TITLE: Serum Polyamine Analysis in Colon and Rectal Carcinoma

PRINCIPAL INVESTIGATOR: Kenji Nishioka

INSTITUTION: University of Texas Health Science Center
San Antonio, TX

ABSTRACT: In preliminary studies, the polyamines (primarily putrescine, spermidine and spermine), recognized as regulators of growth and differentiation of cells, were present in greater amounts in urine and serum of patients with cancer than in appropriate controls. Evidence now suggests that analysis of serum polyamines may serve as a sensitive indicator of solid tumors. We wish to perform serum polyamine assays on patients with carcinoma of the colon and rectum (including Gardner's syndrome), one of the most common solid tumors, and compare such values with serum carcinoembryonic antigen (CEA) determinations from identical sera to correlate the results with the clinical status of patients. Serum polyamines will be measured using an amino acid analyzer while CEA will be determined by radioimmunoassay.

The effects of 5-FU and irradiation on established cell lines of colon carcinoma will be examined, and intra- and extracellular polyamines and CEA content measured. These results will be utilized to interpret more precisely the metabolism and excretion of polyamines found in human sera.

NCI GRANT PROJECT SUMMARY

AREA: Large Bowel Cancer Task Force

GRANT NO.: CA 17168

TITLE: Glycoproteins of Normal and Cancerous Colonic Tissue

PRINCIPAL INVESTIGATOR: W. Ward Pigman

INSTITUTION: New York Medical College
Valhalla, NY

ABSTRACT: The study proposes to investigate the biochemical changes occurring in the secretory and plasma membrane glycoproteins in normal rats and in rats with colonic tumor induced by N-methyl-N-nitrosourea.

Cell suspensions, prepared without the use of enzymes, will be examined for fate of labeled metabolites (glucose, leucine, fucose, etc.). Such cells will also be subjected to fractionation, using discontinuous Ficoll gradient centrifugation. Various glycosultransferase activities in normal and tumorous colonic tissue will also be investigated. Glycoproteins of normal and cancerous colonic tissue will be isolated, purified, and their structural characteristics studied.

Suspending medium (phosphate buffered saline containing mannitol), used for preparing single cell suspension, will be analyzed to identify potential cell aggregation promoting factors.

NCI GRANT PROJECT SUMMARY

AREA: Large Bowel Cancer Task Force

GRANT NO.: CA 19163

TITLE: Assay and Structure of Carcinoembryonic Antigens

PRINCIPAL INVESTIGATOR: Charles W. Todd

INSTITUTION: City of Hope Medical Center
Duarte, CA

ABSTRACT: The goal of this research is to increase the clinical utility of the CEA assay for diagnosis and monitoring of malignant disease. The basic approach being used is to define CEA chemically and to identify distinctive portions of the molecule against which antisera can be prepared. Since research in our laboratory strongly suggests that the antigenic activity of the CEA molecule resides in the protein chain, particular attention will be given to determining the structure of this chain and the synthesis of portions of it for use in immunizations to provoke the synthesis of specific antibody.

NCI GRANT PROJECT SUMMARY

AREA: Large Bowel Cancer Task Force

GRANT NO.: CA 16732

TITLE: Tumor-Associated Antigens in Large Bowel Cancer

PRINCIPAL INVESTIGATOR: Michael D. Turner

INSTITUTION: University of Rochester
Rochester, NY

ABSTRACT: Extensive studies of the carcinoembryonic antigen (CEA) of the human digestive system have failed to establish that this glycoprotein is either tumor specific or confined to entodermal structures, nor has the relation of CEA production to tumor behavior been elucidated completely. It is also not known if the production of abnormal quantities or types of glycoprotein is a phenomenon confined to human colonic cancers or a more widespread feature of these tumors in other species, with perhaps a fundamental role in tumor growth and spread. Efforts directed at explaining the relationship of CEA or other glycoproteins to the malignant process require prospective studies of the time of appearance, location and production of CEA and like substances. Studies of the glycoproteins of existing defined animal models for large bowel cancer, therefore, appear worthwhile.

Tumors will be developed in syngeneic rats using N-methyl-N'-nitro-N-nitro-sequanidin (MNNG) and dimethylhydrazine (DMH) as described by others. Techniques already developed in this laboratory will be used to determine if such cancers produce abnormal glycoproteins analogous to CEA and to establish the time of their appearance in the process of neoplastic transformation and their relation to the biologic behavior of the tumors. If such antigens are detected, later studies will examine their structure and possible role in evoking host response or in protecting the tumor cells from host defenses.

In addition to providing an understanding of CEA production, it is possible that these studies may allow the development of an assay for serum "CEA" in the rat which may be of value in following the effects of therapeutic measures in experimental models of large bowel cancer.

NCI GRANT PROJECT SUMMARY

AREA: Large Bowel Cancer Task Force

GRANT NO.: CA 16724

TITLE: Familial Polyposis: A Clinical and Immunological Study

PRINCIPAL INVESTIGATOR: Samuel A. Wells

INSTITUTION: Duke University
Durham, NC

ABSTRACT: Our objectives in this study are threefold: to determine the incidence of colon polyposis in the family at risk. This will be done by performing barium enemas, sigmoidoscopic and colonoscopic examinations on all family members above the age of 10 years, to perform a multiphasic immunological evaluation of the entire family. This will include the following in vitro techniques: (1) HL-A typing; (2) mixed lymphocyte culture (MLC) reactivity; (3) cell-mediated lympholysis (CML); (4) lymphocyte reactivity to plant lectins, endotoxins, and PPD; (5) T and B cell enumeration; (6) quantitation of chemotactic lymphokine production and quantitation of monocyte chemotactic responsiveness; and (7) quantitation of serum immunoglobulin levels. In vivo studies (cutaneous reactivity to common microbial antigens and to dinitrochlorobenzene (DNCB)) will also be performed.

To evaluate the use of two immunodiagnostic methods: (1) serum carcinoembryonic antigen (CEA) measurement and (2) cutaneous reactivity to the recently described soluble skin reactive antigen (prepared from fetal colon) in detecting familial polyposis and/or adenocarcinoma of the colon.

NCI GRANT PROJECT SUMMARY

AREA: Large Bowel Cancer Task Force

GRANT NO.: CA 15429

TITLE: Detection of Early Colon Cancer

PRINCIPAL INVESTIGATOR: Sidney J. Winawer

INSTITUTION: Memorial Hospital for Cancer and Allied Diseases
New York, NY

ABSTRACT: Cancer of the colon and rectum continues to kill within 5 years more than 50% of the people in whom it occurs even though we now have all the techniques necessary to provide an early diagnosis. We have embarked on a mass screening program for the early detection of colo-rectal cancer and for the identification of patients with premalignant polyps, screening with 6 hemoccult slides on a 3-day, high-bulk, meat-free diet in asymptomatic patients. To date, 6,135 patients have been screened. Compliance has been 85%. The rate of positive slides has been 1%. This represents an 0.9% positivity in patients who had previous examinations at the center, and 1.9% in patients who came for the first time. In most patients only 1 or 2 slides have been positive. Of the 69 patients with positive slides, to date 54 have agreed to further GI studies. Of the 54 who have completed their studies, which included sigmoidoscopy, air-contrast barium enema, and colonoscopy, findings to date are: 26 with adenomatous polyps or villous adenomas; 5 with cancer; 8 with hyperplastic polyps; 10 with diverticulosis; 1 with regional ileitis. Approximately one third of the polyps were detected by colonoscopy and not visualized by barium enema. Directed endoscopic biopsy and cytology have been accurate in the diagnosis of cancers that were observed, but lavage cytology through the sigmoidoscope or colonoscope has not been especially useful. Cytology, isotope incorporation, and enzyme assays are being studied on endoscopically obtained material. In 200 patients screened with previous colon cancer or polyps we have detected 9 polyps and 2 cancers in 9 patients.

NCI GRANT PROJECT SUMMARY

AREA: Pancreas Cancer Task Force

GRANT NO.: CA 18410

TITLE: Oncofetal Antigens in Pancreatic Cancer

PRINCIPAL INVESTIGATOR: Tsann M. Chu

INSTITUTION: Roswell Park Memorial Institute
Buffalo, NY

ABSTRACT: The objective of our proposal is to develop and evaluate an immunodiagnostic method for the detection of pancreatic carcinoma. We will search for pancreatic tumor antigen(s) of oncofetal origin from tumor membrane fraction(s), pancreatic secretions, blood and/or urine of patients with pancreatic tumors. The antigen(s) will further be purified, characterized and specific immune sera will be raised in rabbits and/or guinea pigs. Using the specific antiserum and the purified antigen(s), a radioimmunoassay procedure will be developed in order to determine the blood and/or urine levels of the antigen(s) of patients with pancreatic cancer. To evaluate the immunological activity and specificity of the pancreatic tumor antigen(s), a cell-mediated microcytotoxicity assay will be established. Usefulness of the pancreatic tumor antigen as a marker for the presence of early tumor response to therapeutic treatment, and for monitoring the recurrence of the disease, will be determined.

NCI GRANT PROJECT SUMMARY

AREA: Pancreas Cancer Task Force

GRANT NO.: CA 20115

TITLE: Endoscopic Aspirates of Pancreatic Duct to Detect Cancer

PRINCIPAL INVESTIGATOR: Robert L. Goodale, Jr.

INSTITUTION: University of Minnesota
Minneapolis, MN

ABSTRACT: The research objectives are: (1) to develop rapid, easy and safe method of obtaining human pancreatic fluid at the time of endoscopy; (2) to perform a battery of cytologic, enzymatic, and immunologic studies on this fluid; (3) to study a sufficiently large number of patients with and without pancreatic disease to allow us to form statistically valid comparisons between patients with normal pancreas, pancreatitis, pseudocyst and carcinoma.

The methods entail endoscopy and simultaneous aspiration of pancreatic fluid. Various techniques of brushing and washing of the main pancreatic duct in anesthetized dogs will be evaluated. Noncannulation aspiration devices will also be studied, to be used at the time of endoscopy. The best cytology results will determine the method finally used.

In the clinical studies fluids will be analyzed by polyacrylamide disc-electrophoresis, two-dimensional electrophoresis, and isoelectric focusing with subsequent characterization of abnormal enzyme patterns. In addition, the levels of various serum proteins, i.e., albumin, etc., will be quantitated by the Mancini technique and analyzed further by Ouchterlony gel diffusion and immunoelectrophoresis. Finally, the levels of the two oncofetal antigens, carcinoembryonic antigen (CEA) and alpha-fetoprotein (AFP), will be quantitated.

A group of patients with symptoms of pancreatic disease and a group of patients with occult intestinal bleeding will be studied over three years. A two-year follow-up of each patient is planned. Study of the final results at five years will include a multifactor regression analysis for risk of pancreatic cancer.

NCI GRANT PROJECT SUMMARY

AREA: Pancreas Cancer Task Force

GRANT NO.: CA 19397

TITLE: ACTA-Scan Diagnosis of Pancreatic Carcinoma

PRINCIPAL INVESTIGATOR: John C. Harbert

INSTITUTION: Georgetown University
Washington, DC

ABSTRACT: At the present time the availability of noninvasive diagnostic procedures for the detection of pancreatic carcinoma and for quantitatively measuring changes in tumor size is extremely limited. In this project patients with known or suspected pancreatic carcinoma, ultimately confirmed by biopsy will receive ACTA scans. The results will be compared with other noninvasive diagnostic techniques including ^{75}Se-methionine and ultrasound scans to determine the efficacy of ACTA scanning in the diagnosis and follow-up of pancreatic cancer. Central to this study will be the testing of mechanical and algorithm changes in the ACTA scanner. Attempts will be made to increase resolution by decreasing picture element size, increasing matrix size, decreasing scan section thickness, and altering physical detection parameters to optimize image quality for scanning of the pancreas.

NCI GRANT PROJECT SUMMARY

AREA: Pancreas Cancer Task Force

GRANT CA 20142

TITLE: Origin and Diagnostic Value of Human Serum DNAses

PRINCIPAL INVESTIGATOR: Roger R. Hewitt

INSTITUTION: University of Texas System Cancer Center
Houston, TX

ABSTRACT: The long-term goals of this research are to identify and characterize the deoxyribonucleases (DNAses) in human blood serum with respect to distinguishing enzymatic and physical characteristics, tissue(s) of origin, and qualitative and quantitative variations in activity that have diagnostic value for malignant diseases. Present evidence suggests that the most likely origin for serum DNAse I type activity is the blood leukocytes. These hypotheses will receive special emphasis in this research.

Fluorescence assays have been developed for the quantitation and electrophoretic characterization of DNAses. These assays measure endonucleolytic breakage of PM2 DNA and are sensitive to as little as 1 picogram of DNAse.

Studies will be performed on DNAse activities purified from human blood serum and pancreas. Quantitative and qualitative changes in the DNAse activities in serum from patients with cancer of the pancreas or the hematopoietic system will be evaluated in terms of their diagnostic value.

NCI GRANT PROJECT SUMMARY

AREA: Pancreas Cancer Task Force

GRANT NO.: CA 19652

TITLE: ACTA Scan and Ultrasonography of Pancreatic Diseases

PRINCIPAL INVESTIGATOR: Philip M. Hatfield

INSTITUTION: Lahey Clinic Foundation
Boston, MA

ABSTRACT: A combination of abdominal axial computerized tomography (ACTA scanning) and abdominal ultrasonography will be applied to 200 patients with suspected diagnosis of pancreatic malignancy or pancreatic disease to define sensitivity and specificity of the two diagnostic methods in the detection of early pancreatic disease.

NCI GRANT PROJECT SUMMARY

AREA: Pancreas Cancer Task Force

GRANT NO.: CA 20128

TITLE: Diagnostic Test for Pancreatic Carcinoma

PRINCIPAL INVESTIGATOR: Janis V. Klavins

INSTITUTION: Long Island Jewish-Hillside Medical Center
New York, NY

ABSTRACT: An attempt will be made to develop a diagnostic approach in cases of pancreatic carcinoma. Heterologous antiserum will be raised by carcinomas of pancreas. It will be examined for carcinoma and embryonic tissue specificity. Corresponding antigens will be partially purified. They will be used to raise antibodies reacting with a narrow range of antigens. Such antibodies will be bound in affinity chromatography to obtain sufficient amounts of partially purified antigens for detailed studies. For subsequent investigations purified antigens would be available to raise monospecific diagnostic immune sera.

NCI GRANT PROJECT SUMMARY

AREA: Pancreas Cancer Task Force

GRANT NO.: CA 19232

TITLE: Early Diagnosis of Carcinoma of the Pancreas

PRINCIPAL INVESTIGATOR: William V. McDermott, Jr.

INSTITUTION: New England Deaconess Hospital
Boston, MA

ABSTRACT: Proposed study is designed to evaluate some established methods and to introduce newer techniques in the diagnosis of cancer of the pancreas. Approximately 75 new patients per year will be studied by some combination of the following invasive and noninvasive techniques: (1) Duodenoscopy with cannulation of pancreatic duct, pancreatography and sampling of pancreatic juice; (2) diagnostic radiology utilizing selective arteriography, hepatic vein catheterization and sampling, transhepatic portography and sampling, transhepatic portography with sampling, transhepatic cholangiography, percutaneous transabdominal pancreatic biopsy; (3) ultrasonography utilizing "gray scale" scanning; (4) liver and pancreatic scintiscan; and (5) biochemical and immunological studies on peripheral, hepatic and portal blood including measurement of CEA and antibodies plus selected other "markers" (enzymes and isoenzymes).

Cases will be evaluated as to effect of early diagnosis on survival.

NCI GRANT PROJECT SUMMARY

AREA: Pancreas Cancer Task Force

GRANT NO.: CA 19196

TITLE: Oncofetal Antigen(s) and Carcinoma of the Pancreas

PRINCIPAL INVESTIGATOR: Anastasios Mihas

INSTITUTION: University of Alabama
Birmingham, AL

ABSTRACT: Carcinoma of the pancreas, especially the tail or body, is difficult to detect and diagnosis is almost always too late. The reason for this is the inaccessibility of the pancreas to physical and radiological examination as well. A specific biochemical or serological test would improve early diagnosis and ultimate survival rate of this catastrophic disease. It has been shown that a specific antigen (oncofetoprotein) can be prepared from fetal pancreas and pancreatic cancer tumors. This oncofetal antigen was found in the sera of 37 of 38 patients with carcinoma of the pancreas but absent from healthy controls as well as patients with diseases other than carcinoma of the pancreas.

Antisera to this pancreatic oncofetoprotein will be raised in rabbits by immunization with extracts of fetal pancreas and pancreatic cancer tumors. After evaluation of the antisera, pancreatic carcinoma patients' sera will be tested for the presence of this oncofetoprotein initially by the double-diffusion technique and later on by more sensitive methods such as counter-immunoelectrophoresis and radioimmunoassay. Spontaneous antibodies and anti-antibodies will be sought in the sera of patients with carcinoma of the pancreas, and their blocking or unblocking effect of cell-mediated anti-tumor immune reactions will be studied.

NCI GRANT PROJECT SUMMARY

AREA: Pancreas Cancer Task Force

GRANT NO.: CA 20222

TITLE: Pancreatic Secretory Proteins in Cancer of the Pancreas

PRINCIPAL INVESTIGATOR: Heinrich Rinderknecht

INSTITUTION: University of California
Los Angeles, CA

ABSTRACT: The purpose of this proposal is to analyze pancreatic secretions from patients with normal pancreas, pancreatitis and cancer of the pancreas for specific components or characteristic protein profiles which may assist in the early detection and diagnosis of pancreatic carcinoma. In view of the presumed role of free proteolytic enzymes in development of pancreatitis and possibly cancer of the pancreas and the finding of high concentrations of lysosomal hydrolases at the periphery of invading tumors, we propose to identify and determine some of these enzymes in pancreatic fluid. Their abnormal presence or quantity may indicate existing malignancy or premalignant changes and thus serve as a sensitive diagnostic marker. Clinical and experimental evidence suggests a correlation between diminished levels of pancreatic trypsin inhibitor and pancreatitis. We intend to explore the diagnostic significance of such an association by determining the concentration of trypsin inhibitor in pancreatic secretions of patients with suspected or existing pancreatitis or cancer of the pancreas. A recent study has indicated the existence of a genetically determined polymorphism of human trypsinogen. We shall examine the possibility that preponderance or high levels of one of the two trypsinogen variants may be correlated with a predisposition of a segment of the population to pancreatitis and (or) cancer of the pancreas. We have developed exceedingly sensitive methods capable of detecting pancreatic proteases, trypsin inhibitor and lysosomal hydrolases in the picomole range as well as rapid procedures for the separation of trypsinogen variants and their quantitation which we intend to adapt to the work proposed. Pancreatic fluid will be collected by pancreatic ductal cannulation of patients with suspected pancreatic disease and scheduled for endoscopic retrograde cholangiopancreatography.

NCI GRANT PROJECT SUMMARY

AREA: Pancreas Cancer Task Force

GRANT NO.: CA 19221

TITLE: Retrograde Pancreatic Venography: Animal Autopsy Study

PRINCIPAL INVESTIGATOR: Josef Rosch

INSTITUTION: University of Oregon Health Sciences Center
Portland, OR

ABSTRACT: Objective: Refinement and preparation for clinical use of retrograde pancreatic venography, a method for bettering the diagnosis of pancreatic cancer.

Preliminary studies in animals and man have shown that retrograde pancreatic venography is technically feasible, using transhepatic catheterization of the portal circulation. Proposed animal research will be directed to needed technical refinements and an evaluation of safety. The value of techniques decreasing pancreatic arterial blood flow during the venographic injection of contrast medium and, in particular, the use of vasoconstrictors and/or temporary aortic balloon obstruction will be explored as technical refinements. The safety of pancreatic venography will be evaluated, including the potential risk of induced pancreatitis. Human autopsy and surgical specimens will be studied for a delineation of the normal and pathologic anatomy of the pancreatic venous system, a prerequisite to future clinical use of retrograde pancreatic venography.

NCI GRANT PROJECT SUMMARY

AREA: Pancreas Cancer Task Force

GRANT NO.: CA 19167

TITLE: Laparoscopy in the Diagnosis of Pancreatic Cancer

PRINCIPAL INVESTIGATOR: Paul R. Salmon

INSTITUTION: University of Bristol
Bristol, England

ABSTRACT: Patients with suspected pancreatic cancer will be subjected to laparoscopy in order to inspect and palpate the gland. Suspicious areas, identified by inspection and palpation, will be biopsied under endoscopic control and examined by cytology and histopathology. The results of these studies will be compared with other investigations of the pancreas and an assessment will be made of the accuracy of cancer diagnosis by this technique and of the patients' prognosis during a follow-up period.

NCI GRANT PROJECT SUMMARY

AREA: Pancreas Cancer Task Force

GRANT NO.: CA 19193

TITLE: Pancreatic Tumor-Associated Antigens

PRINCIPAL INVESTIGATOR: Michael D. Turner

INSTITUTION: University of Rochester
Rochester, NY

ABSTRACT: Attempts will be made to identify tumor-associated antigens specific for human pancreatic cancer by immunization of rabbits with saline, KCl and perchloric acid extracts and membrane preparations of human pancreatic carcinomata. Antisera will be absorbed to remove antibodies to normal adult tissue components. Antibodies to tumor-associated antigens will be detected by immunodiffusion, radioimmunodiffusion using labeled antibody, immunofluorescence microscopy, or cross immunoelectrophoresis. To avoid confusion with some previously recognized antigens, the antisera produced will be screened for reactivity with a panel of antigens including CEA, NCA, MTA and alpha-fetoprotein. If tumor-associated antigens more specific for pancreatic cancer can be detected, attempts will be made to isolate and characterize these antigens and to develop radioimmunoassays for them suitable for clinical testing in patients.

NCI GRANT PROJECT SUMMARY

AREA: Pancreas Cancer Task Force

GRANT NO.: CA 19182

TITLE: Pancreatic Carcinoma in Continuous Culture

PRINCIPAL INVESTIGATOR: Adel A. Yunis

INSTITUTION: University of Miami
Miami, FL

ABSTRACT: In our proposed plan we will carry out detailed studies on human pancreatic carcinoma in continuous culture. Three areas of investigation will be pursued: (1) The secretory function of pancreatic carcinoma cells in culture with specific emphasis on the secretion of fibrinolytic activity and procoagulants. (2) Attempts will be made to identify a tumor-specific antigen and methods will be devised for the detection of this antigen and its antibody in sera and duodenal aspirates of patients with pancreatic cancer for possible application in the early diagnosis of the disease. (3) We will test the response of cultured pancreatic carcinoma cells to a wide variety of chemotherapeutic agents singly and in various combinations for possible therapeutic applications.

NCI GRANT PROJECT SUMMARY

AREA: Pathology

GRANT NO.: CA 19122

TITLE: Computer-Assisted Evaluation of Patients with Cancer

PRINCIPAL INVESTIGATOR: Jane Desforges

INSTITUTION: New England Medical Center Hospital
Boston, MA

ABSTRACT: A family of computer programs is being designed to compute the survival value of procedures currently used to stage patients with Hodgkin's disease, and to determine an optimal chronological sequence of these staging procedures for any given patient. These programs, utilizing computational techniques based upon concepts of decision theory, information theory and statistical analysis, will comprise a prototype for a computer-based information system that can be used for any human malignancy for which correlation of clinical findings with tumor extent are known and for which significant benefit is available from therapy determined by extent of tumor.

NCI GRANT PROJECT SUMMARY

AREA: Pathology

GRANT NO.: CA 15125

TITLE: Computer-Assisted Classification of Acute Leukemia

PRINCIPAL INVESTIGATOR: Thomas F. Necheles

INSTITUTION: New England Medical Center Hospital
Boston, MA

ABSTRACT: The primary objective of this proposal is to establish objective and quantitative morphological parameters for the subdivision of classical varieties of acute leukemia. Computer-oriented image processing techniques, developed at this institution for chromosome analysis and, more recently, for an automatic white blood cell scanner and analyzer will be adapted for the analysis of leukemic cells. Slides from 40 children with acute lymphoblastic leukemia will be scanned, the images of 100 leukemic cells from each recorded, and the digitized images analyzed using cell size, color and texture parameters developed for leukocyte analysis and identification. The resulting quantitative morphological data will be analyzed for significant correlation with clinical data including clinical response to specific therapy, overall survival and cure expectancy. Once developed, these techniques can be extended to the field of acute myeloblastic leukemia where clinical results are relatively poor and where many different combinations of therapy exist. The overall goal is to develop objective criteria which may help to identify those patients who will (or will not) respond to a given mode of therapy.

NCI GRANT PROJECT SUMMARY

AREA: Pathology

GRANT NO.: CA 18044

TITLE: Pathology Center for Lymphoma Clinical Studies

PRINCIPAL INVESTIGATOR: Henry Rappaport

INSTITUTION: City of Hope Medical Center
Duarte, CA

ABSTRACT: It is the objective of this project to maintain a pathology reference center and repository and nine regional centers for the purpose of rendering diagnostic and research support to cooperative clinical studies pertaining to the therapy of malignant lymphomas. The pathology reference center and the regional centers are headed by pathologists who have specialized in the diagnosis and study of neoplastic diseases of the lymphoreticular system and are making a joint effort to improve and refine the criteria for diagnosis and classification of these neoplastic diseases, thus to assure the validity of the therapeutic results reported or to be reported by their clinical colleagues engaged in therapeutic clinical studies. A number of ancillary research projects closely related to the primary aim represent endeavors to supplement the work initiated under the auspices of the Hodgkin's disease clinical therapeutic trial study and the lymphoma clinical studies.

NCI GRANT PROJECT SUMMARY

AREA: Prostate Cancer Task Force

GRANT NO.: CA 15502

TITLE: Search for a "Virogene" in Prostatic Tissues and Fluids

PRINCIPAL INVESTIGATOR: William A. Carter

INSTITUTION: Roswell Park ~~Memorial~~ Institute
Buffalo, NY

ABSTRACT: Studies will be directed toward finding -- in human normal, hyperplastic, and neoplastic prostatic tissues and short-term explant cultures -- the presence of viruses, their subcomponents or their expressed functions with properties analogous to those of known oncogenic viruses of other species. In this end, we will employ modern qualitative and quantitative approaches of molecular biology, biochemistry and electron microscopy such as molecular hybridization of cellular nucleic acids with viral RNA, detection in prostatic tissues of reverse transcriptase and -- characteristic for tumor viruses -- high molecular weight RNA, accompanied by ultrastructural and functional definitions of viral particles induced in prostatic explant cultures by halogenated pyrimidines. In addition, we will use highly purified human interferon to distinguish between classes of inducible viral particles as well as to determine its antiproliferative potential against prostatic cells.

Our findings would have far-reaching implications for the etiology of human prostatic cancer and for new practical approaches toward the prevention and possible treatment of neoplastic diseases in man.

BEST COPY AVAILABLE

NCI GRANT PROJECT SUMMARY

AREA: Prostate Cancer Task Force

GRANT NO.: CA 18748

TITLE: Immunochemical Studies of Prostatic Acid Phosphatase

PRINCIPAL INVESTIGATOR: Byung-Kil Choe

INSTITUTION: Wayne State University
Detroit, MI

ABSTRACT: The prostatic acid phosphatase (PAP) is a promising immunological marker enzyme for prostate carcinoma cells. The objectives of our investigations are to define the antigenic specificity of PAP in relation to acid phosphatases of other tissue origin and to develop immunoassay methods for PAP to aid the diagnosis of prostate cancer. We have introduced innovations in the PAP purification procedure which is suitable for immunochemical studies of this enzyme. We have established the immunochemical identity of electrophoretic (or chromatographic) isozymic forms of the PAP. Antigenic specificity of the PAP and the kinetics of PAP-anti-PAP antibody interactions were studied in detail. We have developed counterimmunoelectrophoretic assay and radioimmunoassay for the PAP in the biological fluids and immunofluorescence technique for PAP-secreting cells. These techniques were applied to the determination of serum and bone marrow PAP levels and to the identification of prostate carcinoma cells metastasized to the lymph nodes and bone marrow. Further studies on the antigenic structure of PAP and immunoassays of PAP are in progress.

NCI GRANT PROJECT SUMMARY

AREA: Prostate Cancer Task Force

GRANT NO.: CA 15126

TITLE: Acid and Alkaline Phosphatases in Prostatic Cancer

PRINCIPAL INVESTIGATOR: Tsann M. Chu

INSTITUTION: Roswell Park Memorial Institute
Buffalo, NY

ABSTRACT: The objectives of this proposed research are: (1) to measure acid phosphatase, alkaline phosphatase activities and isoenzymes of alkaline phosphatase in the sera of prostatic cancer patients who are in the chemotherapy trials; (2) to offer uniform laboratory results for clinicopathological correlation between serum acid phosphatase, alkaline phosphatase activities, its isoenzyme patterns and patients' clinical information, in order to evaluate the efficacy of chemotherapy; (3) to establish a serum bank from patients with prostatic cancer.

NCI GRANT PROJECT SUMMARY

AREA: Prostate Cancer Task Force

GRANT NO.: CA 15437

TITLE: Antigen(s) Markers in Diagnosis of Prostatic Cancer

PRINCIPAL INVESTIGATOR: Tsann M. Chu

INSTITUTION: Roswell Park Memorial Institute
Buffalo, NY

ABSTRACT: The overall objective of this project is to isolate and purify antigen markers from human prostatic cancer tissue. The tumor markers will be characterized in their immunological and biochemical properties and a comparison will be made with the other known antigens from other tissue. A radioimmunoassay will be developed for tumor antigen markers in blood and urine and/or prostatic fluid from patients with prostate cancer. Usefulness of the assay as a marker of response to treatment and of monitoring the recurrence of disease in prostatic cancers by follow-up of patients, and establishing an immunological method for detection of prostatic cancer is the ultimate goal of this project.

So far we have isolated and characterized tumor antigens from other tissues. Tumor antigen markers have also been isolated from prostatic fluids and prostatic glands (normal, benign and malignant). The objective for this current year is to purify these tumor antigen markers and to develop an assay procedure (radioimmunoassay) for their measurement in patients' blood and other body fluids.

NCI GRANT PROJECT SUMMARY

AREA: Prostate Cancer Task Force

GRANT NO.: CA 18052

TITLE: Scanning Microscopy of Prostatic Cancer

PRINCIPAL INVESTIGATOR: John F. Gaeta

INSTITUTION: Roswell Park Memorial Institute
Buffalo, NY

ABSTRACT: Scanning microscopy study of prostate disease with emphasis on appearances of cell surfaces and comparison between normal and neoplastic glandular tissue. Study intended to bring out architectural differences that may be significant regarding origin and spread of prostatic cancer.

NCI GRANT PROJECT SUMMARY

AREA: Prostate Cancer Task Force

GRANT NO.: CA 16736

TITLE: Enzymes in Diagnosis and Staging of Prostatic Cancer

PRINCIPAL INVESTIGATOR: John T. Grayhack

INSTITUTION: Northwestern University
Chicago, IL

ABSTRACT: The purpose of this study is twofold; namely, (1) to evaluate the usefulness of enzyme determination in expressed prostatic fluid in identifying patients with a high risk of carcinoma of the prostate; and (2) to attempt to clarify the natural history of carcinoma of the prostate and to determine the value of various clinical procedures to identify the stage of the disease prior to institution of therapy. In an attempt to achieve the first objective, lactic dehydrogenase (LDH) isoenzyme, leucine aminopeptidase, and glucose-6-phosphate dehydrogenase determinations are being carried out in the expressed prostatic fluid of patients; the results of the prostatic fluid studies are being correlated with the clinical and pathologic diagnosis of prostatic pathology. In an attempt to achieve the second objective, patients with a histologic diagnosis of carcinoma of the prostate are subjected to serum acid and alkaline phosphatase determinations and bone X-ray and scan studies. If these are negative or equivocal, pelvic lymph node excisional biopsy is carried out and the nodes subjected to histological study. In addition, random pelvic marrow blood aspiration is performed; the aspirated blood is subjected to acid phosphatase and LDH isoenzyme determination. Simultaneous enzyme determination is carried out on systemic blood. The studies described above are being accomplished at this time. LDH isoenzymes have been determined in 293 specimens. Techniques for the other enzyme determination in prostatic fluid have just been developed. The lymph node-bone marrow studies have been carried out in 20 patients to date.

NCI GRANT PROJECT SUMMARY

AREA: Prostate Cancer Task Force

GRANT NO.: CA 17208

TITLE: GS Antigen in Prostatic Cancer

PRINCIPAL INVESTIGATOR: Phyllis D. Kind

INSTITUTION: George Washington University
Washington, DC

ABSTRACT: P30 antigen has been detected in the prostate of castrated mice by three immunological methods: complement fixation, rocket immunoelectrophoresis, and radioimmunoassay. The antigen has not been detected in extracts of prostate from sham-operated animals. Experiments designed to determine the length of time after castration required for appearance of P30 and to investigate the role of hormones in controlling expression of this antigen are in progress.

NCI GRANT PROJECT SUMMARY

AREA: Prostate Cancer Task Force

GRANT NO.: CA 20118

TITLE: Ultrasonography in the Evaluation of Prostatic Cancer

PRINCIPAL INVESTIGATOR: Martin I. Resnick

INSTITUTION: Wake Forest University
Winston-Salem, NC

ABSTRACT: Prostatic ultrasonography will be carried out in addition to the usual diagnostic studies on patients evaluated for symptoms of bladder outlet obstruction. The scanning technique will be evaluated with regard to three aspects of prostatic cancer: (1) to diagnose early carcinoma in patients with seemingly clinically benign disease; (2) to utilize the technique as a method of accurately staging the extent of the tumor locally; and (3) to evaluate patients treated hormonally for advanced disease in order to accurately detect disease regression and reactivation. Prostatic ultrasonography will be carefully compared with the clinical and histological diagnosis so that positive and negative correlations can be made.

Mr. **ROGERS.** Dr. Carter.

Mr. **CARTER.** We have recently had quite a study on mammography. Will you tell us when that began and when it was reduced in scope and why.

Dr. **UPTON.** Dr. Costlow, would you care to sketch the history of the program.

Dr. **COSTLOW.** Yes. Thank you, Dr. Upton.

To clarify the situation, this was really not a study; it was a demonstration program in the area of screening.

Mr. **CARTER.** Yes.

Dr. **COSTLOW.** That was begun in the midpart of 1973.

Mr. **CARTER.** How many patients were examined with mammography?

Dr. **COSTLOW.** In this program there have been enrolled 281,000 women.

Mr. **CARTER.** Have they all been examined?

Dr. **COSTLOW.** They have all been examined once; a substantial number twice.

Mr. **CARTER.** Recently you reduced the scope of this program. Why?

Dr. **COSTLOW.** Pardon?

Mr. **CARTER.** You are not continuing this in full force any more; is that correct?

Dr. **COSTLOW.** The program is in its fourth year of a 5-year program and we propose to continue to its completion on the basis of advice from four major outside advisers.

Mr. **CARTER.** At the same level?

Dr. **COSTLOW.** Yes, at the same level.

Dr. **UPTON.** Is it not correct that the guidelines were changed?

Dr. **COSTLOW.** Yes, to exclude certain women under age 50 from routine screening. There have been considerable changes in the program.

Mr. **CARTER.** That is what I wanted to know about. You forgot to tell me about those. Why were these changes made?

Dr. **COSTLOW.** They were made as a result of the investigations that Dr. Upton had referred to with regard to the concern over risks to radiation in mammography.

Mr. **CARTER.** As a result of this mammography program, do you think we may well have caused cancer of the breast in many of these women?

Dr. **COSTLOW.** That is difficult to anwer because of the——

Mr. **CARTER.** Difficult to answer; in other words you do not know whether you did or not. You have exposed 281,000 women to three rads. Was that the average amount?

Dr. **COSTLOW.** The average amount per examination today is less than one-half rad.

Mr. **CARTER.** Let's see now. You have reduced the dose recently, but I believe originally it was about 3 rads according to Dr. Upton's statement?

Dr. **COSTLOW.** No. Two rads.

Mr. **CARTER.** I stand corrected. I was one rad off. Two rads are the same as 2,000 millirads, of course?

Dr. **COSTLOW.** Yes.

Mr. **Carter**. Was there a fear because of the sensitivity of breast tissue that you would or probably could have caused cancer?

Dr. **Costlow**. Based on those estimates.

Mr. **Carter**. Yes, sir. And so you reduced the dose as a result of this, not only the rads but the scope of your study; is that not correct?

Dr. **Costlow**. That, is correct.

Mr. **Carter**. Yes, sir. You know we cannot point the finger at anyone many times but we have a power in our hands, the extent of which we know not. We do not know how far it goes. Perhaps we ourselves are causing cancer, and in this case, thousands of cancers.

Do you have any figures to show how many of these 281,000 women you have examined, who do have cancer today, did not have it when you first checked them?

Dr. **Costlow**. No, sir, I do not. I do not know that there is any way to really estimate that.

Mr. **Carter**. You have a record. Surely you are studying that. You will have those figures, won't you?

Dr. **Costlow**. From the radiation levels used in this program I think from a statistical point of view it would be very difficult to isolate any particular case of cancer that arose in this program as a result of X-rays.

Mr. **Carter**. You know that certain cases of breast cancer appeared. You could take a statistically equivalent number and compare them and see whether the increase was statistically significant. You know yourself that you did receive criticism about this program and that you changed it; is that not correct?

Dr. **Costlow**. Yes; that is correct.

Mr. **Carter**. I wanted to be sure about that.

I understand that you can reduce the number of roentgens when you do a CAT scan from 6 to 2, and for a catheterization from 30 to 20 roentgens. You can bring that down, is that correct?

Dr. **Upton**. I would hope that improvements in apparatus would enable us to reduce the exposure associated with cardiac catheterization, yes.

Mr. **Carter**. Could you also reduce the level of radiation in obtaining a CAT scan?

Dr. **Upton**. Yes, sir. I would hope again that improvements in apparatus will reduce those levels in the future.

Mr. **Carter**. Yes, sir. What has been the effect of the injection of radioactive iodine 131?

Dr. **Upton**. Iodine 131 has been shown in experimental animals to produce tumors of the thyroid gland. In the treatment of patients for thyroid cancer with large doses of iodine 131 that destroy the thyroid, there have been observed increases in incidence of leukemia in treated populations.

Mr. **Carter**. You tell it like it is, Doctor. We have many tools but we have to use them wisely and well and we must be especially careful at the outset. We started this technique in about 1942, is that correct?

Dr. **Upton**. With radioiodine?

Mr. **Carter**. Yes.

Dr. **Upton**. Yes, I believe that does go back to the early 1940's.

Mr. CARTER. We have treated 600,000 patients with radioactive iodine and you tell us that this does destroy the thyroid when it is treated for cancer in heavy doses. In lesser doses it may cause tumors or it may cause leukemia. I like your frankness, it is refreshing.

Have you done studies on the use of X-ray for cervical cancer? Do you have any results on the effects of this treatment?

Dr. UPTON. There have been studies supported by the Institute into the possible tumor-causing effects of radiation in the treatment of cervical cancer. Studies have been conducted under the auspices of the Harvard School of Public Health, and to my knowledge these studies have not revealed cancer induction. One would have supposed that the irradiation of the pelvic region might have induced leukemia, since this complication has been observed at lower radiation dose levels in women who were treated for menstrual bleeding. It is my understanding with the larger doses used in the treatment of cervical cancer an excess of leukemia has not been noted.

One should not infer from this that the radiation is without cancer-inducing effects. Rather, I think the circumstances of exposure in this situation may be peculiar. In this situation, one is giving very large doses to relatively small volumes of marrow, and we know from the wealth of evidence that the dose-incidence relationship may rise to a maximum and then come down as the dose is increased further.

Mr. CARTER. Thank you, Doctor.

Really in this case I would believe that from what you say the benefit-cost ratio is favorable. Cancer of the cervix is a very serious disease, and this treatment has been extremely effective. No doubt it does outweigh the disabilities which might occur. Of course, there have been cases where radiation was used for enlarged tonsils with rather disastrous effects, and for cases of acne, and so on.

Dr. UPTON. Yes. We would refer to those situations as malignant treatment for benign disease. We would strongly argue against the use of radiation in such conditions.

Mr. CARTER. Yes, sir. I would agree with you very much on that. I would hope that X-ray is no longer used to treat acne or enlarged tonsils.

Do you think they are still used?

Dr. UPTON. To my knowledge; these applications have been thrown into disrepute and are no longer practiced in this country.

Mr. CARTER. For many years?

Dr. UPTON. Yes.

Mr. CARTER. What do you think about the use of thermoluminescent dosimeters by X-ray technicians or physicians or even patients who are repeatedly X-rayed?

Dr. UPTON. The thermoluminescent dosimeter is enormously helpful in that it can provide a relatively precise measure of the radiation dose and is a simple, small device that allows the radiation field to be well mapped. I would certainly endorse the use of this system of dosimetry for patients and radiation workers as a means of measuring their exposures and recording their exposure histories.

Mr. **Carter**. Is NCI spending enough money researching the health effects of ionizing radiation?

Dr. **Upton**. This is a question that we are seeking to examine now through a working group formed expressly for that purpose. Since the mid-1950's the major effort in the study of radiation effects, including radiation carcinogenesis, has taken place through programs sponsored by the Department of Energy. We now are reexamining the situation, and I think it is fair to say that we will intensify our effort here in coming years.

Mr. **Carter**. What about the use of diathermy; do you have any ill effects from that?

Dr. **Upton**. Diathermy apparatus can, of course, if used incorrectly, give rise to tissue damage through excessive heating. These effects have been well documented.

Mr. **Carter**. What causes the heating?

Dr. **Upton**. It is the absorption of the microwave radiation and the resulting excitation of the molecules of matter in the tissues.

Mr. **Carter**. Resistance causes the heat; is that correct?

Dr. **Upton**. That is correct. The resistance of tissue.

Mr. **Carter**. Do you think this technique is safe?

Dr. **Upton**. It certainly must be used carefully to avoid the thermal damage we spoke about. There is now concern about other kinds of effects, genetic effects, carcinogenic effects. This is a new set of problems which deserves very careful attention. We still do not know what the long-term effects may be of low levels of microwave radiation.

Mr. **Carter**. Have you had any difficulty getting records of individuals exposed to radiation?

Dr. **Upton**. I would like to ask Dr. Boice if he would care to comment on this. He is an epidemiologist and has dealt with this problem himself many times.

Dr. **Boice**. I think it is true that today we are having more difficulty in getting access to certain government records than we did in the past. In 1972 I began a followup study of tuberculosis patients who had received multiple chest fluoroscopies. At that time we had access to the IRS system of records to locate patients who were treated many years in the past. We also had more access to social security records in obtaining notifications that patients were still alive based on their social security number.

It takes a lot longer now to obtain permission from hospitals to access patient records for followup studies. Permission can be obtained but there are a lot more regulations and restrictions than in the past, which I think are justified in terms of confidentiality and privacy. But I think it is true that it is more difficult to conduct followup studies of patients who have been treated in the past with radiation.

Mr. **Carter**. Sometimes I do not know whether it is justified or not to keep those but as long as the true intent of the privacy law is kept, I think it is very necessary to have access to these.

By the way, you brought up an interesting subject regarding the fluoroscopy and the patients who were treated with pneumothorax. Could you describe the effects of fluoroscopy on these patients in the followup? What happened to them?

Dr. **Boice**. Yes. We evaluated over 1,000 women who had received multiple chest fluoroscopies during the 1930's and 1940's. They had received, on average over 100 chest examinations, and their average breast dose was 150 rads of radiation. We did detect a significant excess of breast cancer relating to these procedures. The excess was about a 70-percent increase over what was observed in a comparison group. The comparison group of 700 women had received other treatments for tuberculosis and did not have an excess breast cancer risk.

Mr. **Carter**. Then there is a definite excess. Do you have the percentage or rate of increase?

Dr. **Boice**. There was a 70-percent excess.

Mr. **Carter**. What tissue in the body is the most susceptible, and the most easily provoked by radiation to become cancerous?

Dr. **Upton**. I would think the female breast is now that tissue. This represents a new point of view. In the 1950's the National Academy of Sciences Committee on the Biological Effects of Atomic Radiation evaluated the existing data very thoroughly at that time, and there was no mention then of cancer of the breast as a complication of radiation in the dose range below 1,000 rads. Emphasis was given to leukemia exclusively.

In 1962, the United Nations Scientific Committee reevaluated the available data, and added thyroid cancer to leukemia. Only in the latter half of the 1960's and early 1970's did the comparably high risk of the female breast become evident. I think we would now say that the risk of breast cancer exceeds the risk of radiation-induced cancers of any other tissue of the body.

Mr. **Carter**. Yes, sir. Of course pelvimetry—X-rays of the pelvis, were used many times years ago. Would you have any statement as to what percentage of those fetuses so examined later developed leukemia or other forms of cancer?

Dr. **Upton**. The National Academy of Sciences Committee on Biological Effects of Ionizing Radiation, in its 1972 report, drew attention to the high risks that have been inferred to exist in the unborn child exposed to diagnostic levels of radiation in the mother's womb. The risk estimates held the incidence of leukemia and all other childhood cancers to be increased about 50 percent by a diagnostic exposure *in utero,* to a dose of the order of one rad.

So, if one thinks in terms of relative risks, this relative risk of a 50-percent increase with a dose of the order of a rad, makes the tissues in the fetal stage more sensitive than at any other stage in life. Viewed in that context, certainly the fetus is more radiosensitive to carcinogenesis than the adult female breast.

Mr. **Carter**. What is the latent period between exposure and occurrence of leukemia?

Dr. **Upton**. The average latent period for the development of leukemia in the fetus was estimated to be somewhere in the region of a couple of years. Again, the cancers developing in childhood appear to develop early, and as childhood ranges into puberty, and adolescence, the excess of cancers seems to diminish, even to disappear. But the latency is very much shorter with the childhood cancers than with the cancers of adult life. In adult life, leukemia is thought to have an average latency of perhaps 5 years—cancer of the breast, a latency of perhaps 10 to 15 years or longer.

Mr. CARTER. Yes, sir. There is one other question. What is your feeling about Dr. Radford's testimony to our subcommittee that the current occupational exposure limits should be reduced to 500 millirads?

Dr. UPTON. I understand Dr. Radford's concern, Dr. Carter. I think the question as to what level of occupational risk is acceptable must involve the weighing of risk and benefit; it must involve consideration of the circumstances within the industry under which the risks occur. I think I would agree with Dr. Radford that society should not condone any risks that can be feasibly and reasonably avoided. Whether in fact the occupational standards are too high or too low is not a question that I can readily answer in the context of this discussion, because there are too many other factors that have to be considered.

Mr. CARTER. What types of leukemia are caused by radiation?

Dr. UPTON. To my knowledge, all forms of leukemia except leukemia of the chronic lymphocytic type have been observed to be increased in irradiated populations.

Mr. CARTER. Chronic lymphocytic. That would not include acute lymphocytic?

Dr. UPTON. No, sir.

Mr. CARTER. Of course, these are difficult to classify. Is it easier to tell acute lymphocytic from acute histocytic?

Dr. UPTON. No; that can be difficult, because the immature blood cells are difficult to classify, but chronic lymphocytic leukemia is not a disease that represents a serious diagnostic difficulty. I think that with the very careful followup that has been given to the atomic bomb survivors, patients treated in Great Britain for rheumatism of the spine (ankylosing spondylitis), and other irradiated population groups, had there been an increase in the chronic lymphocytic form, it would have been noted in at least one of those studies. I think this is an interesting observation, because it emphasizes that not only is there a difference in the susceptibility to radiation carcinogenesis among different tissues, but also among the cells—even within the bone marrow or the hemopoietic system—different types of cancer may have evolved through different mechanisms. One cannot treat all forms of cancer in exactly the same way in arriving at estimates of risk.

Mr. CARTER. I notice your therapeutic remissions last a long time in these cases.

Dr. UPTON. Yes, there have been very heartening advances in the treatment of leukemia and lymphoma.

Mr. CARTER. Thank you.

Dr. UPTON. Thank you.

Mr. ROGERS. Thank you.

Mr. Preyer.

Mr. PREYER. Thank you.

We appreciate the testimony of all of you today. I would like to ask Dr. Upton or any of you a question not related to your medical testimony today, but I think it is an important one. I am the chairman of a subcommittee which has jurisdiction over the Privacy Act and over the Freedom of Information Act. I would like to ask you to describe some of the difficulties under the Privacy Act that you might be having in trying to get records that are needed for epidemiological research. If you would rather do that more extensively in the record, that would be fine, but I think this is a problem that is of real concern to us.

Dr. **Upton.** Thank you, Mr. Preyer. I think it would be helpful if we could provide for the record a detailed discussion of this problem area. Certainly, I think none of us see the Privacy Act as intending to hamper legitimate medical research. The question, of course, is how to allow access for legitimate purposes without infringing on the privacy and the rights of the individual. This is an area I have not worked in myself. Again, perhaps Dr. Boice would care to offer comments, since he has dealt with these problems in his own research work.

[The following information was received for the record:]

DIFFICULTIES UNDER THE PRIVACY ACT

There is a vital need for specific information on cancer risks in man, information that can come only from studies of man himself. Whether our concern is with the hazards of the workplace, of our diet, of certain aspects of medical care, of our personal habits, or of changes in our environment, we look to studies of man to identify and measure the risks entailed.

The study of a particular factor for its potential contribution to the burden of human cancer requires linking the records of individuals in systematic fashion, usually over time periods measured in decades, and minimizing the opportunity for bias to operate through self-selection. A cohort of individuals might be defined, for example, as those on the payroll of a plant engaged in a specific chemical process, subdivided as to exposure to the chemical, and followed long enough to determine whether deaths from a specific form of cancer were sufficiently in excess of expectation to infer that the particular chemical might be carcinogenic.

At a time when the demand for information on cancer risks is growing, and it is recognized that even small risks at the level of the individual have important social and economic implications, we should be developing information systems based initially on the extensive data already gathered by Federal agencies for other purposes, and strengthening these systems with other data not now routinely collected. In fact, we are not doing this at all. We are retreating from the challenge to do more with the information in hand and accepting new restraints on access to needed records of individuals in the name of personal privacy. Thus a conflict has arisen between two important social goals, one to provide the information needed to decide social policy, the other to protect personal privacy. With effects on human health increasingly seen as influential factors in decisions on energy and the environment, we find that we lack the information systems that would generate the quantitative data on carcinogenic risks that we need.

Epidemiologists of the National Cancer Institute are experiencing difficulties in gaining access to records for their studies of specific risk factors, and some of these difficulties are increasing as the emphasis on personal privacy spreads throughout government and the private sector as well. An interpretation of the Privacy Act of 1974 led to the termination of the address search service provided by the Internal Revenue Service to medical investigators; subsequently, restrictions were written into the Tax Reform Act of 1976 that put the service beyond their reach. The service had provided medical investigators with current address and date of last tax return, information of the utmost importance in any follow-up study in which further information must be obtained directly from the individuals under study, and helpful also in determining survival. Again, after passage of the Privacy Act, hospitals of the Veterans Administration found themselves unable to contribute information to the cancer registries supported by the NCI as part of its Collaborative Program for Cancer Surveillance, Epidemiology, and End Results Report (SEER Program). The population-based registries of the SEER Program are relied upon for information on incidence, for epidemiologic studies, and for monitoring the effectiveness of cancer diagnosis and therapy. To serve their purpose, every case of cancer in the designated area must be registered, checked for duplication, and followed for survival. Without the input of VA hospitals in a registration area the entire effort is frustrated. Efforts to resolve this problem are continuing but the solution is not yet at hand.

Many studies require access to individual medical records, and increasingly hospitals are unwilling to honor investigators' requests for copies or extracts needed for particular studies. Even private hospitals, not subject to the Privacy Act, cite the Privacy Act as the deterrent. In addition to a widespread misunderstanding of the precise scope of the Act, there has been a movement in state legislatures to enact privacy legislation at the state level, modelled on the Federal Act. Where patient consent has been obtained these difficulties are easily overcome, but obtaining patient consent is often impractical, and in a large study may be impossible.

In mortality follow-up studies, especially of worker cohorts, the National Cancer Institute relies primarily on the Social Security Administration for information on the fact of death, including date and place. Mortality tracing for research purposes is not an integral part of the mission of the Administration, enjoys no high priority in scheduling, and does not make use of all the SSA data that an investigator would want. Typically, a large number of the names in any cohort will be returned to the investigator with the statement that no evidence of death was seen and that death cannot be presumed. Most of the people will be alive, and their SSA earnings record would show this, but such information of survival is not provided to the investigator who must then use other means to determine survival or mortality. Other means are expensive and involve far more invasion of privacy than a check of SSA files. It should be possible, also, for investigators to use SSA earnings records to indicate duration of employment in an industry to refine the exposure classification of the individual, but this information is also beyond the reach of the medical investigator.

In studying particular industries or plants, investigators may be able to get payroll information from individual companies or membership lists from unions in order to define cohorts for follow-up. Where these approaches are not applicable, it should be possible to define rosters on the basis of quarterly earnings reports submitted to the SSA in the appropriate time period.

Information on specific occupation, needed for more refined classification of workers as to exposure, is often very difficult to obtain or inaccessible in a large study. The Bureau of the Census has the best systematic data, but these are not available to the medical investigator. The SSA does not collect information on specific occupation, but the Internal Revenue Service does, and the integration of those data with the SSA information on industry would greatly enhance the potential for making preliminary estimates of health effects of hazards of the workplace.

Dr. **Boice.** I can give one specific example. That involves the Internal Revenue Service. Just a few years ago we were able to access this resource to determine whether persons were alive or not, and what their current address might be. By doing this we were able to locate large numbers of patients nationwide, which is essential when studying low-dose effects, whether for radiation or any environmental exposures. Today we do not have access to the IRS to do research. This is one result of the Privacy Act that has hindered our research somewhat.

Mr. **Preyer.** Well, our subcommittee would appreciate very much any comments you would like to make about problems you are having with it, and also any recommendations that you have on how to deal with the problem that would improve the situation, while, at the same time, considering individual privacy rights. I might ask one question on your statement which may have been covered by this time. I was impressed that you are proceeding with proper caution, and that you are recognizing there is a problem of risk against benefits. And on the benefit side of things, the progress we are making in alternative forms of treatment would have considerable bearing. I wondered if you had any further comments on how realistic alternative techniques such as ultrasound, biological markers in the bloodstream, are; how close we are to having a viable alternative?

Dr. **Upton.** Thank you, Mr. Preyer. I think Dr. Pomerance has indicated that we would hope to be conducting a clinical trial of ultrasound approaches to breast cancer detection which might provide an alternative to X-ray memmography. I think he said we would hope to be able to get that trial underway within a year. So we may be close to an alternative there, depending on how the trial turns out. At least the techniques, in theory, appear to have promise. We are looking extensively into the use of immunological markers, as tests for cancer of the breast and for cancer of the bowel. I think it is still too soon to promise that we are close to an alternative there. But the work is going well. We have promising opportunities to explore. I think there is reason to hope that with further effort we may indeed find immunological, hormonal, and biochemical markers. I do not see them tomorrow, but within a decade we may indeed have a variety of such tests which, used together, may be extraordinarily helpful in diagnosis and detection.

Mr. **Preyer.** So on the ultrasound technique, we may know something, we may have some indication on that within a year?

Dr. **Upton.** We may be able to begin the clinical trial within a year. How long do you think it would take to come to an evaluation?

Dr. **Pomerance.** Approximately 2 or 3 years after onset, after we begin seeing patients with these new pieces of equipment.

Mr. **Preyer.** Thank you very much.

Mr. **Rogers.** Dr. Upton, would you let us know in the record what research is presently being funded by the Institute which may increase our knowledge of the health effects of medical and dental diagnostic X-ray exposure, both good and bad, the levels of funding, number of personnel involved and the initial results?

Dr. **Upton.** We would be happy to do so, Mr. Chairman.

[The following information was received for the record:]

HEALTH EFFECTS OF LOW-LEVEL RADIATION

The National Cancer Institute is spending approximately $5 million on research into the health effects of low-level radiation. This figure includes both intramural and extramural activities in epidemiology and carcinogenesis. Not included in this figure is the support for the Cancer Control Breast Cancer Detection Demonstration projects (BCDDP) nor support for the Radiologic Physics Centers which monitor the BCDDP mammography equipment.

NCI has four epidemiologists on staff who are involved in radiation effects research. In addition to the four professionals, several support staff spend part of their time involved in these activities. Staff in other programs serve as project officers on grants and contracts.

The attached table illustrates some of the epidemiology studies underway and the results of them.

NATIONAL CANCER INSTITUTE

ENVIRONMENTAL EPIDEMIOLOGY BRANCH

RADIOGENIC CANCER STUDIES

MEDICAL EXPOSURES

TITLE	POPULATION STUDIED	RESULTS
1. Breast cancer following multiple chest fluoroscopies	1047 female TB patients repeatedly fluoroscopically examined between 1930-1954 and 717 unexposed comparison patients in Massachusetts	A 78% increased risk of breast cancer was observed among the exposed. Young women were found to be at greater radiogenic risk than old. The risk was present at the end of 45 years of observation. Cumulative low dose fractions carried the same risk as a single exposure of the same total dose. No risk was detected among women over 30 at exposure.
a. Interaction of Radiation with breast cancer risk factors	Questionnaire responses and medical record data of above population	Menarche and pregnancy were found to be times of particular radiosensitivity. Though not significant, women possessing multiple risk factors appeared more sensitive to irradiation.
2. Childhood exposure to radioactive iodine (RAI)	6500 children who received thyroid uptake tests with I-131, 6500 thyroid function test controls, 6500 siblings	Study population being obtained. Preliminary analysis of 1st 1000 exposed show only 1 thyroid malignancy, suggesting low radiation risk. Thyroid cancer, nodules, and hypothyroidism to be evaluated.
3. Radiotherapy for cervical cancer	27,300 women treated with radium, x-rays or both, 2,700 surgical patients. International study involving 29 centers and 10 countries	Preliminary results indicate no leukemia risk--possibly due to high doses delivered to small volume of bone marrow 'sterilizing' cells. Re-activation being considered.
4. Hyperthyroidism treated with RAI	1004 women therapeutically treated with I-131, 2144 surgically treated women at Mayo Clinic 1944-1968	Preliminary mortality analysis suggests no radiation risk. However, followup short and morbidity analysis to be done. More followup being done by FDA/BRH. NCI to assist with analysis.
5. Secondary primary neoplasms after ovarian cancer	Survey of 70 medical centers and SEER registries to evaluate carcinogenicity of alkylating chemotherapy and irradiation	Possible excess colon and bladder cancer associated with large radiation exposures.

Mr. ROGERS. In the breast cancer detection program, how many centers do we have currently operating?

Dr. COSTLOW. Twenty-seven centers are currently operating.

Mr. ROGERS. Do they all operate under the same methods, same rules?

Dr. COSTLOW. Yes, sir, they do. We have a uniform manual of procedures and operations.

Mr. ROGERS. How long has that been the situation?

Dr. COSTLOW. That has been the situation at least since February of 1977, when the first copy of the work scope, which was actually a contract requirement rather than guidelines, was put into the field.

Mr. ROGERS. How long were the guidelines uniform before that?

Dr. COSTLOW. The whole program, from its inception, has been a kind of evolutionary thing. I think the very nature of demonstration programs causes that kind of flexibility. There were uniform protocols as guidelines established at the outset. Perhaps Dr. Pomerance could comment more on those, because he was involved in the beginning, but as of early 1977 we did have uniform ones set down.

Mr. ROGERS. That was because it was a requirement of the contract.

Dr. COSTLOW. Yes.

Mr. ROGERS. In other words, you just did not leave it to the judgment of those involved.

Dr. COSTLOW. No.

Mr. ROGERS. You said you had to agree to this in the contract if we fund you.

Dr. COSTLOW. That is right.

Mr. ROGERS. Which was not necessarily carried out, then, by those centers in the beginning of the program.

Dr. COSTLOW. No. I think there were specific contract requirements, that they were developed into a more uniform procedure over a period of a couple of years before they were actually instituted as a contract work-scope.

Mr. ROGERS. Were you telling me that all of those centers had uniform practices before the contract requirement of February 1977?

Dr. COSTLOW. Well, no. In the very beginning they did not have uniform ways of reporting. There was a uniform way of doing the examinations.

Mr. ROGERS. Why was it at Georgetown they were exposing them to three times the recommended maximum dosage?

Dr. COSTLOW. Early on, the centers for radiological physics only got involved with this program in 1975, that is their first report. The centers for radiological physics were not involved at the very inception of the program. It was only then we began to look at those things through the centers.

Mr. ROGERS. Seventeen were producing radiation levels that were ominously high. So there was not much uniformity, I do not think we could claim, was there?

Dr. COSTLOW. No, there was not uniformity in that respect, because there was no monitoring in the beginning through those centers.

Mr. ROGERS. Although you had guidelines.

Dr. COSTLOW. There were guidelines.

Mr. ROGERS. Did the guidelines go to exposure levels?

Dr. COSTLOW. No, they did not. I think the guidelines in the very beginning were relatively vague, in the sense that they described the techniques to be used as medically acceptable.

Mr. ROGERS. But now what do you do?

Dr. COSTLOW. Now we have specific guidelines with specific limitations on the radiation dosage, knowing we can monitor these things on a biweekly basis. With annual comprehensive surveys of all the equipment, we can and have done that in fact as an actual contract requirement.

Mr. ROGERS. In other words, the only way you could get this brought about and changed was to require it in the contract.

Dr. COSTLOW. That is correct.

Mr. ROGERS. Now, are there any guidelines or ways of enforcing these guidelines for screening programs that are not affiliated with the National Cancer Institute.

Dr. COSTLOW. That probably goes beyond the purview of our program. We have confined our efforts to this project.

Mr. ROGERS. So there is no way for you to know about the others; is that right?

Dr. COSTLOW. That is right.

Mr. ROGERS. Is there any reporting from the nonfunded NCI programs to you?

Dr. COSTLOW. No, sir, but we have an interagency agreement with the Bureau of Radiological Health, have shared with them our knowledge about this program, and have shared through our centers for radiological physics the developed technology for measuring X-ray exposure and through their—BRH—BENT program and others get into the area of radiation beyond this program.

Mr. ROGERS. What line of communication do you have with the nonaffiliated screening centers? How many of those exist? Do we know?

Dr. COSTLOW. We really do not know that. The only communication we would have is just by the dissemination of the information we have in our own in terms of guidelines and indicate that our own program is following these specific guidelines.

Mr. ROGERS. So as far as we know there may be screening programs going on that are still giving three times exposure rates.

Dr. COSTLOW. I think that is a possibility, although——

Mr. ROGERS. What responsibility has the National Cancer Institute, not only for controlled programs, but for prevention-of-cancer programs? Is that not also yours? As I recall, we wrote that into the act.

Mr. CARTER. Mr. Chairman?

Mr. ROGERS. Yes.

Mr. CARTER. If you will yield on that, it appears that this is really a local problem, the whole thing, the way I see it. I regret it.

Mr. ROGERS. Could you answer the question?

Dr. COSTLOW. I am sorry—would you repeat the question?

Mr. ROGERS. Would the reporter read the question?

[The reporter read the record as requested.]

Dr. COSTLOW. Yes, we do have responsibility for prevention programs, that is true.

Mr. ROGERS. That is what I wonder now. If these centers are conducting screening programs, do we have any responsibility to help prevent women under 50 being exposed and excessive radiation being used in the mammography program?

Dr. COSTLOW. Yes, I certainly think we do.

Mr. ROGERS. What are we doing to carry it out? You did not even know how many such screening programs there were.

Dr. UPTON. May I try an answer to this?

Mr. ROGERS. Certainly.

Dr. UPTON. The 27 breast cancer detection demonstration projects are, in our view, model programs that are an effort to provide models for others to follow. The centers for radiological physics, in collaboration with the Bureau of Radiological Health and its BENT—breast exposure nationwide trends—program according to Dr. Pomerance, now do involve over 80 percent of the mammography equipment in the country. So, there is in fact through this mechanism an effort underway to bring the techniques used for X-ray examination of the breast into some sort of conformity with the best of modern methods today.

There is clearly some difference in purview here between the National Cancer Institute and the Bureau of Radiological Health. The Bureau of Radiological Health sees its role as having to do with guidelines for medical practitioners at large. Clearly the breast cancer demonstration projects which were started in the Cancer Institute gave us new experience that must be the basis for the improvement of techniques on the national level. And the efforts of our Division for Cancer Control and Rehabilitation are intended, indeed, to bring about as quickly as possible reduction of radiation dosage to the minimum and restriction of the mammographic procedures to those in whom the benefit can be expected to outweigh the risk, and then to disseminate this information for national use.

Mr. ROGERS. And what means do we have to see that those nonaffiliated screening groups are carrying out the guidelines? Do we have any mechanism?

Dr. UPTON. The Bureau of Radiological Health has been surveying and monitoring. So I think that information is available to us. I regret to say I do not know what that information shows at the present time.

Mr. ROGERS. What has the Cancer Institute done to contact the Bureau of Radiological Health to see that this is brought about?

Dr. UPTON. We have been meeting regularly with the Bureau to discuss this program and related issues.

Mr. ROGERS. But would you put in for the record what has happened, the discussions held, what actions have been taken?

Dr. UPTON. Be happy to.

[Testimony resumes on p. 926.]

[The following information was received for the record:]

NATIONAL INSTITUTES OF HEALTH INTERAGENCY AGREEMENT

There is close liaison and exchange of information among NCI, BRH, and the Center for Radiological Physics (CRP) supported by DCCR. The CRPs have shared newly-developed technology and instrumentation for measuring radiation exposure that are now being applied by BRH in the Breast Exposure: National Trends (B.E.N.T.) program. This effort is being accomplished through State Health Departments which now include voluntary participation by 42 States. It is anticipated that all 50 States will eventually participate.

National Institutes of Health
Interagency Agreement

ISSUING OFFICE National Cancer Institute Cancer Control Contracts Section Research Contracts Branch, OD Blair Bldg. Room 201, Silver Spring, Md. 20910	**AUTHORITY** CPH 224-77-[illegible] Economy Act of 1932 as amended (31 U.S.C. 686) Agreement For: Mammography Quality Assurance Program	**TYPE OF CONTRACT** Cost Reimbursement
CONTRACTOR *(Name and Address)* Bureau of Radiological Health of the Food and Drug Administration 12720 Twinbrook Parkway Rockville, Md. 20852	**ACCOUNTING AND APPROPRIATION DATA** CAN No 7-8423282 ($150,000) Subobject Class 25.1T Doc. No. Y1CN70602	
PLACE OF PERFORMANCE Rockville, Maryland	AGREEMENT AMOUNT $300,000--Subject to the terms and conditions of ARTICLE IV--Total Funds Allotted: $150,000	
MAIL VOUCHERS TO See Billing Instructions	**SPONSOR** Division of Cancer Control & Rehabilitation	
	EFFECTIVE DATE November 1, 1976	**EXPIRATION DATE** September 30, 1978

The Agency agrees to furnish and deliver all the supplies and perform all the services set forth in the attached Special Provisions, for the consideration stated stated herein. The rights and obligations of the parties of this Agreement shall be subject to and governed by the Special Provisions. To the extent of any inconsistency between the Special Provisions and any specifications or other provisions which are made a part of this contract, by reference or otherwise, the Special Provisions shall control

Food and Drug Administration NAME OF ACCEPTING AGENCY	National Cancer Institute NAME OF SPONSORING AGENCY
BY George E. Berry SIGNATURE OF AUTHORIZED INDIVIDUAL	BY SIGNATURE OF CONTRACTING OFFICER
George E. Berry TYPED NAME	David M. Keefer TYPED NAME
TITLE Deputy Dir., Div. of Contracts & Grants Management	11/12/76 DATE
DEC 6 1976 DATE	

HEW-554 (7/70)

THIS AGREEMENT CONSISTS OF:

1. COVER PAGE

2. CONTENTS OF AGREEMENT

3. SPECIAL PROVISIONS
    PREAMBLE
    ARTICLE I SUBSTANCE OF THE AGREEMENT
    ARTICLE II DESCRIPTION OF WORK
    ARTICLE III PERIOD OF PERFORMANCE
    ARTICLE IV CONSIDERATION
    ARTICLE V TECHNICAL REPORTING
    ARTICLE VI PROJECT OFFICER
    ARTICLE VII BILLING PROCEDURES
    ARTICLE VIII NONEXPENDABLE PROPERTY
    ARTICLE IX PATENTS

PREAMBLE

The Bureau of Radiological Health (BRH) of the Food and Drug Administration (FDA) conducts a national program to reduce unnecessary exposure of the population to ionizing and nonionizing radiations. To this end, the Bureau (1) develops criteria and recommends standards for safe limits of radiation exposure, (2) develops methods and techniques for controlling and reducing radiation exposure, (3) plans and conducts research to determine health effects of radiation exposure, (4) provides technical assistance to agencies responsible for radiological health control programs, (5) develops and disseminates recommendations and educational programs concerning medical radiation practices, and (6) conducts an electronic product radiation control program to protect the public health and safety.

Because ionizing and nonionizing radiations are useful modalities in the diagnosis and treatment of many types of cancer, and because the National Cancer Institute (NCI) is responsible for developing techniques for the diagnosis, treatment, and control of cancer which may involve increased radiation exposure of the public, which itself may increase cancer risk, continued cooperation is necessary between FDA and NCI in order to identify and quantify radiation exposure problems associated with these techniques and to support programs to minimize unnecessary radiation exposure and maximize benefit. Because of continuing BRH activities in the estimation and reduction of the radiation exposure required to obtain diagnostic information, it is essential that continuing collaboration with NCI on these matters be established.

ARTICLE I

SUBSTANCE OF THE AGREEMENT

A. GENERAL

Whereas, the Food and Drug Administration (FDA), hereinafter referred to as the "Agency," and the Division of Cancer Control and Rehabilitation (DCCR), National Cancer Institute (NCI), National Institutes of Health (NIH), hereinafter referred to as the "Sponsor," desire to enter into an Agreement for the support of nationwide activities to reduce unnecessary patient exposure from mammography and to improve image quality; and

Whereas, the work and services to be conducted by the Agency under this Agreement will be performed on a two (2) year basis. Establishment of program support activities for the Mammography Quality Assurance Program, nationwide implementation through collaboration with State and local radiological health agencies, and development of more comprehensive quality assurance procedures and test tools will require approximately one(1) year, and expansion of program activities including implementation of improved followup procedures will require approximately one (1) additional year, totaling a two (2) year program.

B. OBJECTIVE - The Agency is to provide State and local readiological health agencies with program support for the implementation of the Mammography Quality Assurance Program; to make available training for professionals (State surveyors, medical physicists, technologists, radiologists) in quality assurance procedures; to develop and field test tools for the reduction of unnecessary patient exposure and the improvement of image quality.

NOW, THEREFORE, the parties do agree as follows:

ARTICLE II

DESCRIPTION OF WORK

A. During FY 77 FDA shall:

1. provide sufficient support for State and local radiological health agencies to implement the Mammography Quality Assurance Program. This will include the following items.

   a. dosimetry cards and TLD support for both initial screening and subsequent mailings of TLD's.

   b. compilation and analysis of the data.

   c. training of State surveyors by FDA personnel in mammography survey techniques and recommended quality assurance procedures for facilities.

2. provide two followup survey kits for each FDA region to be used in diagnosis and correction of apparent processing and beam quality errors.

3. develop a mammography survey protocol for State and local radiological health personnel, including x-ray generator and processing parameters which should be measured, appropriate test tools, and acceptable limits of variation. Work conducted by Centers for Radiologic Physics (CRP's) and other interested parties will be considered during the development of these procedures.

4. develop and field test facility based quality assurance procedures and test tools (including a phantom) in order to assess and maintain image quality in all mammographic facilities. Work conducted by CRP's and other interested parties will be considered during the development of these procedures.

5. produce training materials, such as written manuals, video tapes, self-learning packages, etc., illustrating mammography survey techniques and mammography quality assurance procedures to be used in the instruction of Federal, State, local, and other radiological personnel.

6. conduct a training course for the FDA Regional Radiological Health Representatives to act as an interface with State programs and to conduct direct training of State personnel through training sessions at Regional meetings and in individual States, as necessary.

7. appoint a Project Review Committee (PRC), including members nominated by the Sponsor, which will meet periodically to review progress of the Agreement.

8. maintain liaison with appropriate Task Groups of the CRP's in order facilitate consideration of their work in Agency programs.

B. During FY 78 FDA shall:

1. continue program support and training activities for remaining States to implement the Mammography Quality Assurance Program.

2. update followup survey kits and improve protocols for followup surveys with quality assurance procedures and test tools which have been developed. Additional followup survey kits will be made available to State programs.

3. provide for dissemination of program results and developed quality assurance procedures and test tools to mammography facilities and physicists through additions to the Radiological Health Sciences Learning Laboratory, training packages for radiologic technologists, and other training materials, as appropriate.

4. update membership of PRC as appropriate.

5. maintain liaison with appropriate Task Groups of the CRP's in order to facilitate consideration of their work in Agency programs.

C. NCI shall:

1. provide for transfer of any pertinent information and technology from NCI research and control acitivities.

2. provide for the coordination of the six CRP's to serve as a scientific resource in the development and implementation of the mammography quality assurance programs.

ARTICLE III

PERIOD OF PERFORMANCE

Performance of this Agreement shall begin on November 1, 1976, and shall not extend beyond September 30, 19 78 unless otherwise modified. Initiation of the Mammography Quality Assurance Program in approximately one-half of the Radiological Health Agencies (approximately 9 per quarter beginning January 1, 1977) and the development and field testing of quality assurance procedures and test tools will be completed by September 30, 1977.

Initiation of the program in the remaining Radiological Health Agencies (dependent upon State capabilities), improvement and expansion of followup surveys, and dissemination of information developed on quality assurance procedures and test tools will begin on or about October 1, 1977 and will be completed by September 30, 1978.

ARTICLE IV

CONSIDERATION

A. For performance of this Agreement, the Sponsor agrees to reimburse the Agency in the estimated amout of $300,000 .

B. Total funds currently available for reimbursement and allotted to this Agreement are $150,000. Further allocation of funds hereunder will be accomplished at the option of the Sponsor, depending upon the progress and the results of the work and services performed during FY 77, and consistent with the time that approval to proceed with the work proposed for FY 78 has been granted by the Sponsor.

C. It is estimated that the amount of funds currently allotted under B above will cover performance of the work to be accomplished during FY 77, which is scheduled to be completed by September 30, 1977.

ARTICLE V

TECHNICAL REPORTING

A. The Agency shall submit to the Sponsor's Project Officer five (5) copies of a semiannual progress report, including a description of work performed during the period reported upon, statistical summaries ofgrouped State data, projections for the following period, and problems, if any, within 15 days after the reporting period; and twenty (20) copies of a comprehensive final report at the end of the Agreement.

B. The Agency shall also submit semiannually, a brief summary of salient results to date and a summary of the final report upon completion or termination of the Agreement.

C. In all Agency publications resulting from work performed under the Agreement, the Agency shall acknowledge support of the National Cancer Institute under this Agreement.

ARTICLE VI

PROJECT OFFICER

The Project Officer representing the Agency for the purpose of this Agreement is Dr. Ronald G. Jans

The Project Officer representing the Sponsor for the purpose of this Agreement is Dr. Winfred F. Malone.

The Project Officer is responsible for: (1) Monitoring the Contractor's technical progress, including the surveillance and assessment of performance and recommending to the Contracting Officer changes in requirements; (2) interpreting scope of work; (3) performing technical evaluation as required; (4) performing technical inspections and acceptances required by this contract; and (5) assisting the Contractor in the resolution of technical problems encountered during performance. The Contracting Officer is responsible for directing or negotiating any changes in the terms, conditions, or amounts cited in the contract.

ARTICLE VII

BILLING PROCEDURES

A. The Accounting Operations Branch of FDA shall submit Standard Form 1080 annotated with the Agreement number to:

Contracting Officer
Cancer Control Contracts Section
National Cancer Institute
Blair Building, Room 201
National Institutes of Health
Bethesda, Maryland 20014

B. Upon inception of the Agreement, billing shall be done on an advance basis in order to insure timely obligation of funds and will be credited to FDA Appropriation No./ Appropriation and Allotment Numbers to be supplied by FDA/

BEST COPY AVAILABLE

C. Administrative billing requirements shall be in accordance with GAO Policy and Procedures, Title 7, Section 8.4.

ARTICLE VIII

NONEXPENDABLE PROPERTY

A. All items of nonexpendable property to be required by the Agency for use in direct performance of this Agreement, shall require the prior written approval of the Sponsor's Contracting Officer.

B. Title to all nonexpendable property acquired under performance of this Agreement shall vest and remain in the Agency.

ARTICLE IX

PATENTS

The Agency will assume responsibility for protecting the interests of the United States Government in matters relating to patents.

BEST COPY AVAILABLE

Mr. ROGERS. I would like staff to query the Bureau of Radiological Health and give us a report as to how many center screening programs are going on that are not affiliated and what is the actual condition as to carrying out the guidelines.

[The following information was received for the record:]

It has not been determined how many active screening centers exist for X-ray mammography outside NCI programs. The estimated number of mammography units is about 3,000. These units would be used for diagnostic purposes (where symptoms or other indications for mammography exist) as well as for routine screening on an individual basis. It is anticipated that the voluntary program, through the BRH, will be effective in encouraging the prudent use of X-ray mammography and controlling the exposures to radiation by frequent surveillance of the instruments used. Even though the program is voluntary, the early evidence indicates that the proportion of nonparticipants is quite small.

Mr. ROGERS. Should we allow breast or other screening programs which do not follow the guidelines?

Dr. UPTON. Mr. Chairman, in my view if the guidelines have been developed for our screening projects, they are based on what we hope is sound logic, and I would trust, therefore, that the same logic should be applicable elsewhere, to other institutions and other programs. There may, of course, be extenuating circumstances that obstruct uniform applicability. But if so, I am not aware of them.

Mr. ROGERS. It is my understanding that there may be 4,000 sites where they have the capability, at least, of conducting the screening and the diagnostic testing. So we really have a rather large area to see if guidelines are being followed. I think some action should be taken. I hope you would have immediate discussions with the Bureau of Radiological Health, and if you should have problems in certain areas, they should be brought to the attention of the Congress.

Would you do that?

Dr. UPTON. Yes, sir, indeed. These discussions are proceeding, and we will act on your advice.

Mr. ROGERS. I notice here an "Urgent Message," I think you probably may be aware of this, put out by ACS/NCI Screening Center in New York City. This is from the Professional Education Department of the American Cancer Society. Are you aware of this bulletin that they put out?

Dr. COSTLOW. Yes, sir.

Mr. ROGERS. Do you know about when that was issued?

Dr. COSTLOW. I guess about a year and a half ago.

Mr. ROGERS. Is it still being issued?

Dr. COSTLOW. Not that I know of.

Mr. ROGERS. Has there been another bulletin issued?

Dr. COSTLOW. The bulletins that have been issued from the Cancer Society have pretty much reflected the changes that we have instituted in the breast cancer program.

Mr. ROGERS. Because I notice that all of these seem to be changed now from what your latest requirement would be, because you say now you would not want a woman under 50 to have mammography unless she had a history of cancer. This, I think, goes beyond that.

Dr. COSTLOW. Yes, it certainly does go beyond that.

Mr. ROGERS. And also this says, "Yes, she should have if at any age she has concern and mammography is recommended by her physician." That is a rather broad guideline, I would think, which is contrary to what you say the guideline is that you have put into effect now.

Dr. UPTON. Our guideline pertains to routine screening. We would not routinely advise women under 50 to be screened. But if the physician finds a reason to recommend it, we do not want to contravene the advice of the physician.

Mr. ROGERS. I understand that. But I do not know that you should say "if at any age she has concern." Is that the basis, that she has some concern, is that the basis then for the physician to recommend it?

Dr. UPTON. I would not think that is sufficient basis alone.

Mr. ROGERS. But that seems to be rather a large loophole in the guideline. This is evidently published by the American Cancer Society. Is this still being applied anywhere?

Dr. COSTLOW. No, sir. As you know, they are cosponsors of this breast cancer screening program with us. They have concurred with the recent evolutionary change that we have had in the guidelines as a result of new information.

Mr. ROGERS. So now they also are taking the position that women under 50, unless they have a history of cancer, should not have a mammography unless the physician himself determines it?

Dr. COSTLOW. I presume so, because I have seen no evidence to the contrary from their published literature.

Mr. ROGERS. Have you seen them publish any bulletin to that effect?

Dr. COSTLOW. No, I have not.

Mr. ROGERS. Would you let us know? I presume there is rather close liaison.

Dr. COSTLOW. Yes, there is.

Mr. ROGERS. Have you published anything to go to other centers?

Dr. COSTLOW. To our centers, yes.

Mr. ROGERS. No, I mean to other centers as well.

Dr. COSTLOW. No, we have not.

Mr. ROGERS. Or to physicians, dentists?

Dr. COSTLOW. No, sir.

Dr. UPTON. Was there not a report on the breast cancer consensus meeting which was widely disseminated and which included the new guidelines?

Dr. COSTLOW. Yes. That is what I was about to say. The new revised guidelines that are in use in this program have been widely distributed throughout the country, as well as the results of the consensus panel that was held last September.

Mr. ROGERS. Well, now, I understand, following the issuance of the revised NCI guidelines for participation in the program, the percentage of women under age 50 who were still participating was quite large, was it not?

Dr. COSTLOW. When the guidelines were first revised, they did include a few more of the risk factors than we now include.

Mr. ROGERS. How many were participating after the revision?

Dr. COSTLOW. After that, the distribution of ages over and under 50 in this program was about half and half.

Mr. ROGERS. I understand there were about 75 percent of women under 50 who were still participating after the revision of that.

Dr. COSTLOW. That is correct, after the August 1976 revisions, which were not as tight as the ones now.

Mr. ROGERS. How many are now participating under age 50?

Dr. COSTLOW. Now less than 15 percent, perhaps down to 12 to 14 percent. This is within the expected range of those who would fall into those risk categories.

Mr. ROGERS. Did the Cancer Society object to any of the tightening of the regulations?

Dr. COSTLOW. No.

Mr. ROGERS. Any of the—I did understand that three members of NCI went to New York and visited with the American Cancer Society for revision of the first guidelines and came back and they were somewhat relaxed. Was that true?

Dr. COSTLOW. I am not familiar with that. I was not involved with that meeting.

Dr. POMERANCE. Mr. Chairman, it is my impression that there may be some discrepancy. The statement that you read from, I believe, and, of course, I have not seen it at this moment, is a statement that was issued by the New York City Division of the American Cancer Society. It was not issued by the American Cancer Society and the American Cancer Society, as far as I know—and I think Dick can corroborate that—never altered the rules that were established by the NCI. These were suggestions, I believe, of the New York City Division of the American Cancer Society.

Mr. ROGERS. Yes, I think that is, that is the American Cancer Society, the New York City Division.

Dr. POMERANCE. It is not the American Cancer Society. That is——

Mr. ROGERS. Also, it is the ACS/NCI Screening Center in New York City.

Dr. POMERANCE. This may have been issued individually by them, but was not issued by the American Cancer Society at any time. The American Cancer Society never indicated that it stood behind those suggested regulations, to my knowledge.

Mr. ROGERS. Now, I thought the New York City Division was a part of the American Cancer Society.

Dr. POMERANCE. It is.

Mr. ROGERS. But you distinguish between them? In other words, someone operating and using the name of the American Cancer Society in one State is not the American Cancer Society?

Dr. POMERANCE. I do not know what their charter regulations are, Mr. Chairman, but I would presume that situation is probably correct as you just described it.

Mr. ROGERS. I would think not. What would make you think that it is not the American Cancer Society if it says it is, and it just says it is the New York Division of it?

Dr. POMERANCE. Well, I do know that that was issued by the New York City Division.

Mr. ROGERS. Of the American Cancer Society.

Dr. POMERANCE. But never received approval of the American Cancer Society. My only reason for responding in the way that I am, Mr. Chairman, is to indicate to you that the American Cancer Society never took the position that was contrary to the National

Cancer Institute in terms of running the particular breast cancer demonstration projects.

Mr. ROGERS. Well, then, as I understand it, you are saying that although every State's cancer society may be issuing different things, somebody, somewhere else who calls themselves the American Cancer Society never did it.

Dr. POMERANCE. Mr. Chairman, you see I am putting myself in the difficult position of trying to defend everything that happens in the American Cancer Society. I do not want to do that. I am trying to indicate to you that the American Cancer Society, as such, with which the National Cancer Institute dealt—the National Cancer Institute never dealt with the New York City Division of the American Cancer Society. It did deal with the American Cancer Society, the national organization.

Mr. ROGERS. Did you not know that this message which the New York City Division of the American Cancer Society issued states on it "The ACS"—American Cancer Society—"NCI"—National Cancer Institute—"Screening Center in New York City which provides free examination to women is: Guttman Institute," so on. In other words, this says, "Here are the guidelines," and refers to the ACS/NCI.

Dr. POMERANCE. I am not endorsing that. I would condemn it as much as you are condemning it, Mr. Chairman. Again, I want to make the point that this was not a national effort. What you see there is a local effort, New York City.

Mr. ROGERS. Is the ACS/NCI screening center a local effort?

Dr. POMERANCE. Yes, sir, a local effort in New York City.

Mr. ROGERS. That screening center.

Dr. POMERANCE. Screening center.

Mr. ROGERS. Did we fund it?

Dr. POMERANCE. Yes, we did.

Mr. ROGERS. Did these guidelines apply to it?

Dr. COSTLOW. No, sir, they did not. I can assure you that. The contract that the NCI has with the Institute referred to there in New York has been following the guidelines since their inception.

Mr. ROGERS. Your guidelines permitted women under 50 to be screened?

Dr. COSTLOW. Originally, yes.

Mr. ROGERS. That is what I am saying.

Dr. COSTLOW. But as we began to change those guidelines—as the result of newer information and the convening of these conferences—we instituted these changes in the contracts to which all of those contractors have responded.

Mr. ROGERS. You did not know that? You have not really made them respond until February of 1977, is what you told me, by contract?

Dr. COSTLOW. Well, that is when the contract was modified; that is correct.

Mr. ROGERS. But when did you say this was issued, about 1976?

Dr. COSTLOW. I think it was about a year and a half ago. I do not remember the exact date of that. But I think it did originate from the New York Division or a subdivision of the American Cancer Society. The people who represent the American Cancer Society with whom we have dealt are representatives of the national organization.

Mr. ROGERS. Do they let any division change guidelines?

Dr. COSTLOW. I do not know, sir.

Mr. ROGERS. Do you allow it in your screening?

Dr. COSTLOW. No, we did not.

Mr. ROGERS. Well, he says it is a local thing. These were guidelines that the local group put out.

Dr. COSTLOW. It is my understanding that center was in progress before the involvement with the National Cancer Institute.

Mr. ROGERS. It lists ACS/NCI Screening Center right on this bulletin.

Dr. COSTLOW. Yes, I know that. But what I am saying is that I do not think what they have published there reflects the views of the national organization of the American Cancer Society, and there has never been a reissuance of that message that I know of.

Mr. ROGERS. I do not know whether there has been or not. It may still be being carried out. You said you do not know whether there has been another to counteract it.

Dr. COSTLOW. Yes, there has been.

Mr. ROGERS. We would like to see them. You told me you did not know if another bulletin had been issued counteracting this.

Dr. COSTLOW. By the Cancer Society?

Mr. ROGERS. Yes.

Dr. COSTLOW. Their (the ACS) agreement with the guidelines as we have instituted them all the way along, that is the national organization I am talking about, would have not conflicted with that.

Mr. ROGERS. The local programs with the cancer people, do you find local autonomy to deviate from your guidelines?

Dr. COSTLOW. Not the centers that we are responsible for.

Mr. ROGERS. Well, you are responsible for these and any guidelines that you say the national puts out. Now, you are telling me only those centers you have joint control of? Dr. Pomerance said well, now, the American Cancer Society, that is the only ones we dealt with, we did not deal with any individual groups underneath them. Now you are telling me the only control you have is those where you have money. Now, which is which?

Dr. POMERANCE. All of them are established through the national organization. The money, the sharing of the funding was through the national organization. It had no relationship——

Mr. ROGERS. It did not go to this screening center?

Dr. POMERANCE. The Guttman Institute was picked, it had no relationship to the New York City Division of the American Cancer Society.

Mr. ROGERS. They are putting out the bulletin telling them to go there.

Dr. POMERANCE. Well, they were not authorized to do that.

Mr. ROGERS. Not authorized by whom?

Dr. POMERANCE. By anyone, either by the National——

Mr. ROGERS. Then how did it ever get done?

Dr. POMERANCE. The New York City Division thought it wise to put it out.

Mr. Rogers. In other words, you are saying that the local programs have the autonomy to deviate from anything they want?

Dr. Pomerance. No. Dr. Costlow stated they do not. I want to state that they never did have. They could not deviate.

Mr. Rogers. But they did.

Dr. Pomerance. That is an individual event——

Mr. Rogers. An individual event which affects some thousands of women.

Dr. Pomerance. I do not know that Guttman Institute has officially indicated its acceptance of those guidelines.

Mr. Rogers. You do not know that they have not, either, do you?

Dr. Costlow. Yes, I can attest to that, they have.

Mr. Rogers. What?

Dr. Costlow. They do not support that——

Mr. Rogers. As of when?

Dr. Costlow. As of at least August of 1976.

Mr. Rogers. As of August?

Dr. Costlow. Yes.

Mr. Rogers. Or February of 1977?

Dr. Costlow. Well, August of 1976 was when the first guideline was revised. It was not until——

Mr. Rogers. I thought you said that is when this one was published. This is the revised guideline.

Dr. Costlow. No, that is not. That is not the revised guideline for NCI/ACS program. The guidelines that were issued in August, even as far back as August of 1976, were published with the cooperation of the American Cancer Society and condoned by them and supported by them. I do not know what position the Cancer Society now has with regard to that document that you hold. All I know is that the centers, even that center that is involved with the National Cancer Institute program, has been following the guidelines.

Mr. Rogers. Well, do you mean to tell me you are running a program, you are dealing with the American Cancer Society, and you permit their individual groups to issue different guidelines?

Dr. Costlow. I do not think I had any control over that at the time.

Mr. Rogers. I thought you said it is a joint program between ACS and NCI.

Dr. Costlow. Well, it is, but that document does not reflect any authorization with the joint program, is what I am saying, even though it says that there.

Mr. Rogers. It says it.

Dr. Costlow. This must have been done at the institution of a subgroup of the Cancer Society.

Mr. Rogers. Well, it is a subgroup, it says the American Cancer Society, the "Professional Education Department, American Cancer Society, New York City Division, 19 West 56th Street, New York, N.Y."

Well, I think you had better, for the record, put all of the bulletins issued, all of the agreements between NCI and the American Cancer Society on this program, please submit those to the committee.

Dr. Costlow. I will be happy to do that.

Mr. **Rogers.** Giving us the various guidelines, when they were changed, when you were aware of any changes made by the American Cancer Society, and also the standards followed by the various programs, which guidelines.

[Testimony resumes on p. 945.]

[The following information was received for the record:]

MODIFICATION #2 TO THE SCREENING GUIDELINES FOR THE BCDDP

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

NATIONAL CANCER INSTITUTE

SENT TO ALL BCDDP PROJECT DIRECTORS

October 21, 1977

OUR REFERENCE: OM #8-77

Dear Dr. .

SUBJECT: Modification #2 to the Screening Guidelines for the BCDDP

This letter and the enclosed screening guideline modification constitute Operational Memorandum #8. The guideline modification is effective immediately and will become an integral part of the Manual of Procedures and Operations of the Breast Cancer Detection Demonstration Project. These new guidelines are no longer interim, but will be implemented until the end of the five-year screening period unless you are notified otherwise. These guidelines result from recommendations made by the NIH/NCI Consensus Development Meeting for Breast Cancer Screening held on September 14-16, 1977. A copy of the recommendations of the Consensus Development Panel is also enclosed for your information.

As soon as practicable, you will receive a printed and perforated copy to insert into your Manual. This Operational Memorandum represents a modification to your contract and is approved by the NCI Contracting Officer.

Sincerely yours,

Richard D. Costlow, Ph.D.
Project Officer, Breast Cancer
Detection Demonstration Project
Division of Cancer Control and
Rehabilitation

Approved by:

Contracting Office, RCB, NCI
Enclosure
cc: Project Coordinator

Operational Memorandum #8
Breast Cancer Detection Demonstration Project
October 21, 1977

MODIFICATION #2
to the
Screening Guidelines for the Breast Cancer Detection Demonstration Project

This operational memorandum addresses issues discussed and recommendations made by the NIH/NCI Consensus Development Panel for Breast Cancer Screening, which met at open session at NIH on September 14-16, 1977. This modification to the screening guidelines for the Breast Cancer Detection Demonstration Project (BCDDP) will be effective immediately and will remain in effect until further notice. These new guidelines are no longer considered interim and will be effective until the end of the five-year screening period unless you are notified otherwise. In implementing these guidelines, there should be clear understanding that, "Throughout its deliberations, the Panel repeatedly emphasized the distinction between mammography -- used for diagnosis...the value of which was not in question...and mammographic screening to detect possible disease in women who have no symptoms or physical findings whatsoever."

At the NIH/NCI Consensus Development Meeting for Breast Cancer Screening, the Panel made a number of recommendations pertaining to screening being conducted in the BCDDP. One of those recommendations was to continue the BCDDP to completion of the five-year screening program, which the NCI intends to do. For implementing this recommendation, the following guidelines are effective immediately for the BCDDP.

Mammography:

1. Women 50 years of age (current age) or older may be given mammographic examination as a part of the routine screening process, provided that appropriate informed consent is obtained.

2. For all women 40 through 49 years of age (current age), routine annual screening by mammography will be discontinued except where there exists:

    a. A personal history of breast cancer, or

    b. A history of breast cancer in the screenee's immediate family (mother/sisters).

3. Women 35-39 years of age may be given mammography in this Project only if they have a personal history of breast cancer. All other routine mammography screening in this age group will be discontinued.

4. All women, regardless of age or whether or not they may receive a mammographic examination, should be maintained in the Project for history and physical examination for the five-year screening period.

BEST COPY AVAILABLE

Follow-up:

For enrolled women with the diagnosis of cancer, long-term follow-up will be instituted, as recommended by the Consensus Panel, and procedures will be determined to complete this follow-up. It was recommended by the Working Group for the Review of the BCDDP that normal screenees not be followed over a long term since there would be no scientific value in following women for a five-year period beyond the screening. NCI has not adopted final recommendations for BCDDP on this point. You will be informed in March 1978 of planned procedures for long-term follow-up, after discussion by the Cancer Control and Rehabilitation Advisory Committee in February 1978.

Informed Consent:

A new consent form is being developed, in keeping with recommendations by the Consensus Panel. The issue of offering routine mammography to women of any age who request it, after being fully informed of risks and benefits, has not yet been fully resolved at NCI. Until a new consent form is developed and a decision is made addressing this issue, you should (1) administer the current consent form for all screenees and (2) continue to honor only written requests from the screenee's physician, as you have been doing since May 1977 for mammography screening in women less than 50 years of age.

Thermography:

The Consensus Panel stated that "Because the potential benefits of thermography remain undocumented, the Panel recommended that thermography be discontinued as a routine part of the BCDDP screening program except in those centers where sufficient expertise is available to justify further clinical investigation and research. Because thermography in the BCDDP was not set up as a research study, its continued use should require the development of a research design."

We will be discussing with each Project the use of thermography as a routine screening modality and the advisability of continuing it in certain projects to gain additional information. These discussions with individual projects will take place over the next three months. Until the decisions are made, you should continue screening with thermography as in the past.

Quality Control Procedures:

The Consensus Panel recommended that "the histology of any lesion smaller than one centimeter in diameter, or any papillary or intraductal proliferation originally interpreted as malignant, be reviewed by at least two pathologists prior to definitive therapy.

"Women who have been screened already and who have had a diagnosis of cancer should be notified promptly if there has been a change in diagnosis."

BEST COPY AVAILABLE

This is interpreted as a recommendation for concurrent pathology review in the BCDDP. The complexity of implementing the concurrent review and the necessity for notifying women of persistent discrepancies in diagnosis will require further discussions with the Working Group for the Review of the BCDDP and with the Projects. Institution of these procedures is expected within the next few months.

The Working Group for the Review of the BCDDP recommended, in addition to concurrent review of pathology, a concurrent review of mammography and monitoring of quality of the physical examinations. These issues will also be discussed further with the Review Group and the Coordination Working Group to develop specific procedures for implementation.

Reporting:

Monthly reporting for mammographic screening will continue as before (See Operational Memorandum #6, May 1977), but should include separately the age groups 35-39, 40-49, and 50 and over.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

NATIONAL CANCER INSTITUTE

May 3, 1977

OUR REFERENCE: OM #6-77-

(THIS LETTER TO BE SENT TO ALL BCDDP DIRECTORS (cc: Coordinators), DMC & Drs. Markel & Holleb, ACS)

Dear Dr.

SUBJECT: Modification #1 to the August 23, 1976 Interim Guidelines

This letter and the enclosed screening guideline modification constitute Operational Memorandum #6, are effective immediately, and will become an integral part of the Manual of Procedures and Operations of the Breast Cancer Detection Demonstration Project. As soon as practicable, you will receive printed and perforated copy to insert into your Manual. This Operational Memorandum represents a modification to your contract and is approved by the NCI Contracting Officer.

Sincerely yours,

Richard D. Costlow, Ph.D.
Project Officer, Breast Cancer
Detection Demonstration Project
Division of Cancer Control and
Rehabilitation

Approved by:

David M. Keefer
Contracting Officer

Encl.: as stated

cc: Project Officer

Operational Memorandum #6
Breast Cancer Detection Demonstration Project
May 3, 1977

MODIFICATION #1

To The

August 23, 1976 Interim Guidelines

This operational memorandum discusses events pertinent to the issuance of guidelines for screening and provides the modifications to screening that were developed during a Project Directors' Meeting on April 20 and 21, 1977. Modification #1 to the August 23, 1976 Interim Guidelines will remain in effect until further notice. This modification applies to routine screening in the Breast Cancer Detection Demonstration Project and is not intended as a guideline for the general medical practice.

Background:

The August 23, 1976 Interim Guidelines resulted from the consideration of recommendations provided in the preliminary reports of two of the Expert Groups commissioned by the Director of the National Cancer Institute (NCI). Following the issuance of the August 23, 1976 Interim Guidelines, the NCI established a Working Group for the Review of the Breast Cancer Detection Demonstration Project (BCDDP). A primary objective was to ascertain what scientific information could be obtained from the BCDDP that would reflect possible gains achieved in the current use of mammography in screening for breast cancer since the time of the Health Insurance Plan (HIP) study. This Working Group first met in January 1977 and a preliminary report is expected in early summer.

In early March 1977, final reports were received from all three Expert Groups. These included a review of radiation risks, a review of HIP pathology, a review of HIP benefits, and a summary of recommendations all of which were distributed to all Projects. NCI is reviewing these reports and these, as well as the reports from the BCDDP Working Group, will be among the basic considerations at an NIH Breast Cancer Screening Consensus Meeting to be held in September 1977.

On April 8, 1977, a preliminary report was obtained from the BCDDP Data Management Center (DMC) that provided the first opportunity to gain some perspective on how the BCDDP centers have implemented the August 23, 1976 Interim Guidelines with regard to screening women with mammography. These data, for the period September 15 - December 15, 1976, showed some problems in providing an exact perspective of implementation in individual projects. The overall screening rate in screening women 35-49 years of age showed a downward trend but was not consistent throughout the Projects. As a first step, NCI submitted these data to each project for validation and to reconsider the individual Project approach to implementation of the August 23, Interim Guidelines. Second, NCI and the DMC corrected obvious

BEST COPY AVAILABLE

problems in the data and provided the April 20 tabulation for discussion at the April 21 and 22 Project Directors Meeting. The discussions produced additional insight to project operations, such as: (1) the period covered by the tabulation was a period of transition and subsequent tabulation of more recent months will show further downward trends in screening rates; (2) the tabulated data did not reflect dropouts due to "fear of mammography" and/or women who were asymptomatic with previous negative screening(s) and saw no reason to return. In this latter area, dropouts for any reason, could be significant because a count of screening report packages received each month during 1976 implied that screening had dropped from a high of 24,000 prior to July 1976 to a low of 17,000 in the later months of 1976. Third, on May 3, the tabulated data and overall screening situation, along with available alternatives, was presented to the Cancer Control and Rehabilitation Advisory Committee which independently concurred with the following modifications:

Modified Interim Guidelines and Reporting:

The following guidelines will be put into effect immediately.

1. For all women 35 through 49 years of age (current age), routine annual screening by mammography will be discontinued except for the following situations:
    (a) A personal history of breast cancer.
    (b) A history of breast cancer in the screenee's immediate family (mother/sisters).
2. Women 50 years of age (current age) or older may be given mammographic examination as a part of the screening process provided that appropriate informed consent is obtained.
3. All women, regardless of age or whether or not they may receive a mammographic examination, should be maintained in the project for history, physical examination, and thermography as well as for the projected post-screening, long-term follow-up.

The Informed Consent Record (Form 91, Version 5) will continue in use and all screenees must read, understand, and sign the form. The statement "I do ( ) I do not ( ) wish to accept the mammographic examination at this time" is not relevant for those women 35 through 49 years of age who will not be given the mammographic examination and should be blocked out. This statement is relevant and should be completed for: (1) all women 50 years of age and older; and (2) those 35 through 49 years of age where mammography may be given according to criteria cited in the statement labeled No. 1 of this modification.

At the project physician's discretion, written requests from physicians outside the project for mammographic examinations of enrolled screenees of any age may be honored. It is understood that such requests are not frequent. These requests should be documented as part of the screenee's file and a record of these requests should be maintained at the project site.

Each Project shall submit monthly tabulations to NCI separately for the age groups (current age) 35 through 49, and 50 and older that provides: (a) total number of women who were scheduled for screening, (b) total number of women returned and screened by any modality, and (c) of those screened, the total number of women receiving mammograms. A sample table format is attached for your guidance. Please continue to keep a log in your Project of the medical indications for all screening by mammogrephy in women 35 through 49 years of age.

These guidelines will be incorporated in your contractual Statement of Work (Manual of Procedures and Operations).

Project No. ________
Location ________
Reporting Mo. ________
(No./Yr.

BREAST CANCER DETECTION DEMONSTRATION PROJECT

Monthly Project Report

GROUP I: 35-49 age group (current age)

a. Number of screenees due* for annual screening during this calender month ________

b. Number of screenees returning and receiving one or more of the examinations as part of their annual screening during this calender month ________

c. Number of screenees receiving mammographic examinations as part of annual screening during this calender month ________

d. Percentage receiving mammograms of those scheduled (c ÷ a x 100) ________%

e. Percentage receiving mammograms for those who returned and were screened by any modality (c ÷ b x 100) ________%

GROUP II: 50 and over age group (current age)

a. Number of screenees due* for annual screening during this calender month ________

b. Number of screenees returning and receiving one or more of the examinations as part of their annual screening during this calender month ________

c. Number of screenees receiving mammographic examinations as part of annual screening during this calender month ________

d. Percentage receiving mammograms of those scheduled (c ÷ a x 100) ________%

e. Percentage receiving mammograms for those who returned and were screened by any modality (c ÷ b x 100) ________%

* "Due for annual screening" includes all screenees expected to return as established by their initial (1-1) annual screening when considering delays and re-scheduling of annual screenings due to the introduction of either an early recall or delayed appointments. Thus, the entered numbers I-a and II-a will reflect screening load prior to guidelines and will include dropouts for any reason.

BEST COPY AVAILABLE

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

NATIONAL CANCER INSTITUTE

Dear Dr: (This letter has gone out to all Project Directors and Coordinators of the Breast Cancer Detection Demonstration Projects - August 23, 1976)

The purpose of the Breast Cancer Detection Demonstration Projects (BCDDP) was to demonstrate the ability to recruit, screen, and follow a population of 270,000 asymptomatic women for the early detection of breast cancer. Screening procedures included history, physical exam, mammography and thermography in all women. The original purpose of recruitment and initial evaluation has been accomplished and has resulted in the detection of many breast cancers.

As you are aware, the value of mammography in totally asymptomatic women under the age of 50 has been questioned. The value of mammography for screening in women over the age of 50 years seems established. There is no question as to the value of mammography as part of the diagnostic workup for symptomatic women of any age. The American Cancer Society and the National Cancer Institute believe that the BCDDP Project Directors must have guidance for a course of action until all final reports are submitted to NCI and have been evaluated by the NCI. These include the reports of Drs. Upton and Thomas.

In addition, many of the Project Directors have requested an evaluation of benefit derived from the BCDDP's. In order to begin this evaluation, we will be reviewing carefully the entire demonstration project with special reference to those cases detected by mammography alone.

The Director of the National Cancer Institute and the President of the American Cancer Society concur with the following guidelines.

1. For women of any age in which there is a suspected breast neoplasm, mammography is an accepted part of the complete diagnostic workup.

2. For asymptomatic women over 50, definite benefit from adding mammography to physical examination has been demonstrated. Mammography is indicated as part of a regular screening program.

3. For asymptomatic women ages 35-50 years, the benefit of the sophisticated types of mammography currently available have not been in common use long enough to demonstrate its benefit in reducing mortality in the screened population. It is by no means clear that there is no benefit. In younger women with evidence of being at special risk of breast cancer, the techniques employed may have value in detecting early breast cancer.

4. The possible risk of inducing a breast neoplasm by the mammographic procedure itself is assumed, but for any individual woman is very small, e.g., as stated by Dr. Upton "...a single mammographic examination with the newer low-dose technique, which involves a dose of one rad or less, would be expected to increase a woman's lifetime risk by no more than one percent. Hence, since the risk from natural causes that the average woman will develop breast cancer during her lifetime is roughly one in fifteen, or seven percent, a single mammographic examination might increase her lifetime risk from 0.07 to 0.0707; by the same token, it would take 100 examinations to double her lifetime risk--that is, to raise it to 0.14. Because the incremental risk per examination is small relative to the individual's lifetime risk from natural causes, a woman should not be reluctant to have a mammogram if there are medical or psychological grounds for desiring the information it could provide. On the other hand, although the presumptive risk to a single individual may be small, the total risk to a large population of healthy women might not be justified unless outweighed by the expectation of a commensurate benefit."

5. Thus, the following interim guidelines are prudent. We cannot recommend the routine use of mammography in screening asymptomatic women ages 35-50 years in the NCI/ACS BCDDP at this time. However, in the face of a very small presumed risk for any individual woman, we do not recommend withholding mammography from a woman age 35-50 years if she and the physician agree that it is in her best immediate interest.

6. For women at high risk because of family history, reproductive history, prior breast cancer, or tumor, etc., the benefits as well as the possible risks of x-ray mammography should be fully explained to the woman concerned and the final decision made between her and the physician.

7. As with any x-ray examination, radiation dosage must be kept to the lowest dose consistent with good image quality. All screening participants should be informed that the x-ray equipment in the BCDDP program is regularly monitored to determine the radiation exposure levels and these levels are reviewed by experts in radiation physics.

8. Women of any age who decline mammography should be encouraged to continue in the screening program for history, physical examination, and thermography.

9. Regardless of the final recommendations, you and your screenees should know that there is no intention to close or phase out the BCDDP's. It is also to be noted that the screening program could be modified in the future in the event of development of new scientific information.

We want to repeat that these are interim guidelines. We appreciate fully that there may also be a risk in depriving asymptomatic women under the age of 50 of potential benefit to them as individuals. On the other hand, given the possibility of even low risk to large numbers of such women, we feel that above guidelines are most prudent until such time as additional current data can be further analyzed.

If any questions arise, please contact Dr. Fink, (301) 427-7996; Dr. Hamner, (301) 427-8057; Dr. Costlow, (301) 427-7993; or Dr. Holleb, (212) 371-2900.

Sincerely yours,

Diane J. Fink, M.D., Director
Division of Cancer Control and
Rehabilitation

Arthur I. Holleb, M.D.
Senior Vice President for Medical
Affairs and Research
American Cancer Society

cc: Mr. Lane Adams
Dr. William Markel
Mrs. Jean Weddle
Dr. Theodore Cooper
Dr. Donald Fredrickson
President's Cancer Panel
NCAB
American College of Radiology
Dr. Lester Breslow
Dr. Arthur Upton
Dr. Louis Thomas
Bureau of Radiological Health

Mr. ROGERS. Particularly an urgent message like this one would get the women, I would think, to say: "Here is the thing to do, go here to the ACS/NCI Center."

Now, I understand that.

Who is the chief medical officer of the American Cancer Society, would you know?

Dr. COSTLOW. The chief medical officer——

Mr. ROGERS. Is Dr. Arthur——

Dr. COSTLOW. Dr. Arthur Holleb represents them; yes, sir.

Mr. ROGERS. Now, I understand within the last 18 months in the publication C.A., he urged relaxation of standards. Are you aware of that?

Dr. COSTLOW. Yes, sir, I am. But we did not relax the standards in the program.

Mr. ROGERS. I understand the past president of the ACS also urged the same thing in a Reader's Digest article.

Dr. COSTLOW. Yes, sir.

Mr. ROGERS. But you say that has no bearing on what they do, not your guidelines, but theirs.

Dr. COSTLOW. Their guidelines had no bearing on what was conducted in the programs which we supported.

Mr. ROGERS. But you do not know what is happening outside your programs?

Dr. COSTLOW. That is true in terms of other screening centers.

Mr. ROGERS. You do not know whether your guidelines are being followed or ACS may have changed its guidelines and everyone just picks out their own guidelines, is that it?

Dr. COSTLOW. I think that may have been on an individual basis.

Mr. ROGERS. Do you not think we ought to know, with the responsibility we have for prevention of cancer, what is happening out there?

Dr. COSTLOW. Yes, I think we should.

Mr. ROGERS. Would you check into it and let this committee know immediately?

Dr. COSTLOW. Yes, sir.

Mr. ROGERS. Now, in October 1977, in the statement of recommendations and of consensus developed on breast cancer screening, there is a statement on page 3,

> Panel members concluded BCDDP's may have an ethical obligation to continue to offer mammography to women under 50 enrolled in the program if it is made clear to them through informed consent that the benefit has not been proved, that there is presumed risk, and the panel does not recommend its routine use for this age group.

Dr. UPTON. I am sorry, Mr. Chairman.

Mr. ROGERS. I would like for you to comment on the finding of the consensus development panel for breast cancer screening program which was issued October of 1977. And here is what it says on page 3:

> Panel members concluded that BCDDP's may have an ethical obligation to continue to offer mammography to women under 50 enrolled in the program if it is made clear to them through informed consent that the benefit has not been proved, that there is presumed risk, and the panel does not recommend its routine use for this age group.

Dr. UPTON. Yes, I would be happy to comment on that.

Mr. ROGERS. All right.

Dr. UPTON. As I recall, the panel was divided over the question, and I think the majority of panel members were opposed to the expenditure of taxpayers' dollars to provide screening to younger women when in fact the estimates of relative magnitude of benefit, as opposed to risk, suggested that the procedure could be deleterious.

There were, on the other hand, members of the panel who argued that women had enrolled in the program with the expectation that they would receive five successive annual X-ray mammographic examinations, and that we had, in a sense, entered into a contract with such women to give them examinations. And because the risks of the examination were presumably small—that is, the examination might not increase the woman's natural risk any more than a small percentage—it was thought that one should not deny the woman the examination if she did in fact request it. There were in a sense, then, two ethical imperatives acting in opposite directions: One should defer to the wishes of the patient if she wanted the examination, given evidence that it might not be beneficial, on balance.

Mr. ROGERS. Is that the general prevailing view?

Dr. UPTON. I think the Institute took the position that it could not assent to the expenditure of taxpayers' dollars to provide mammography to women under 50. If they wanted the procedure, they should receive it elsewhere, and not through one of our centers. Dr. Costlow may correct me on that.

Dr. COSTLOW. That is correct. That is the position in this program. We do not honor that request, that us a request by the individual.

Mr. ROGERS. In other words, you do not allow the patient to be the one to decide this matter.

Dr. COSTLOW. That is correct.

Mr. ROGERS. Any more.

Dr. COSTLOW. That is right.

Mr. ROGERS. As of February of 1977-78.

Dr. COSTLOW. When the newest guidelines were published.

Mr. ROGERS. February of 1978?

Dr. COSTLOW. The correct date is October 1977.

Mr. ROGERS. So since October the individual woman is saying: "I would like to have it," if she is under 50, would she not?

Dr. COSTLOW. That is right. Prior to that, that question was never raised.

Mr. ROGERS. Because she could, she could get it prior to then?

Dr. UPTON. If she was under 50 without risk factors.

Dr. COSTLOW. Without risk factors.

Mr. ROGERS. Yes. I think it would be well to let the committee have a rundown on what is happening in all of the areas. As you say, there are only 20 percent of the machines that are not within our own centers. What was that figure, Dr. Pomerance?

Dr. POMERANCE. It is indicated, of the 4,000 to 5,000 pieces of equipment that you correctly indicated were being used for mammography in this country, 80 percent of them, at the last go-around I am aware of, in the reporting from the Bureau of Radiological Health, had been monitored at least once. I think it might be interesting to know that in the second go-around of monitoring they reported that the dosages in these nonaffiliated NCI mammographic centers or offices that were using equipment for mammography, that the dosages, the average dosage was approximately the same as the average dosage in BCDDP's.

Mr. ROGERS. Which is 1 rad?

Dr. POMERANCE. That is correct.

Mr. ROGERS. Per breast.

Dr. POMERANCE. There has been excellent educational involvement.

Mr. ROGERS. So we still have 20 percent that we are not checking.

Dr. POMERANCE. The Bureau of Radiological Health does not have any policing qualifications, I believe. These are all voluntary.

Dr. UPTON. When we spoke with the Bureau of Radiological Health this year, they reported at that time they had 42 States involved in this program, and they were seeking to extend their coverage to all 50 States.

Mr. ROGERS. You say that this can now be done at about 200 millirads?

Dr. UPTON. Yes. The figures I have now are that the following are average values for two views of each breast: in the standard examination with the film-screen procedure, the average midline dose is 71 millirads, and with the xeroradiographic procedure it is 570 millirads; or 0.071 rads in the case of the film screen system, and 0.57 rads for the Xerox system, substantially less than 1 rad in either case.

Mr. ROGERS. Now, are you saying, Dr. Pomerance, 80 percent of the machines now are in that degree?

Dr. POMERANCE. Yes.

Mr. ROGERS. So in this Nation now, 80 percent of these machines are operating in exposing women with this procedure, mammography, to less than 200 millirads, is that what you have stated?

Dr. POMERANCE. I believe so.

Mr. ROGERS. Are we sure?

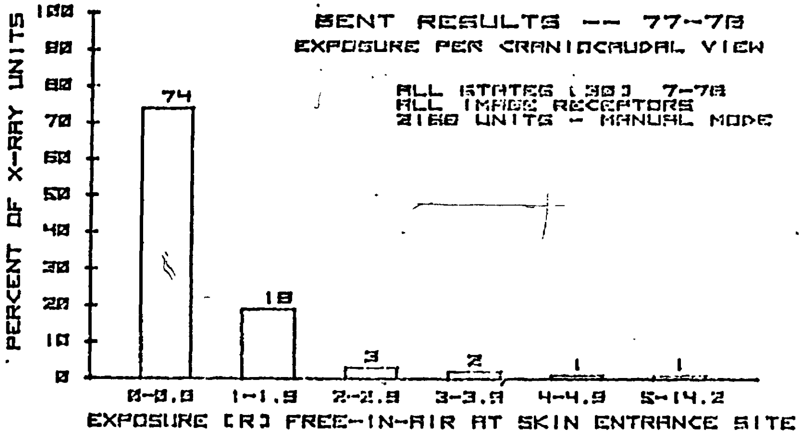
Dr. POMERANCE. Well, I am reporting from my last recollection of the BENT report. Their report indicated at that time, and it may have been the prior report for the BCDDP's, that the reference was made to, that the average dose was at least as good as the average dose of the BCDDP's.

Mr. ROGERS. Would you confirm that for us for the record?

Dr. POMERANCE. Yes, sir.

[The following information was received for the record:]

BREAST EXPOSURE: NATIONWIDE TRENDS (BENT)



BEST COPY AVAILABLE

Mr. ROGERS. Did the ACS oppose at all the tightening of guidelines?

Dr. COSTLOW. There was debate at open forum.

Mr. ROGERS. Did you have any correspondence with them?

Dr. COSTLOW. No, sir.

Mr. ROGERS. No correspondence on this issue at all?

Dr. COSTLOW. On this issue we kept them informed of the development of our guidelines as we went along.

Mr. ROGERS. Did they submit anything in open session to the changes?

Dr. COSTLOW. Not that I recall, in writing. In open debate there were some concerns expressed about the possibility of overtightening——

Mr. ROGERS. What about the editorials in their journal?

Dr. COSTLOW. They published a few of those.

Mr. ROGERS. Would you make available for the record any correspondence?

Dr. COSTLOW. I certainly will.

Mr. ROGERS. And any express written opinions like editorials in the Journal of American Cancer opposing the tightening of the guidelines.

Dr. COSTLOW. Yes, sir.

[Testimony resumes on p. 1032.]

[The following material was received for the record:]

CORRESPONDENCE AND RELATED MATERIALS OPPOSING THE TIGHTENING OF GUIDELINES BY AMERICAN CANCER SOCIETY

AMERICAN CANCER SOCIETY, INC.
777 THIRD AVENUE • NEW YORK, N.Y. 10017 • (212) 371-2900

WILLIAM M. MARKEL M.D.
VICE PRESIDENT FOR SERVICE
AND REHABILITATION

RESEARCH
EDUCATION
SERVICE

February 4, 1976

Mr. Allan C. Benton
Contract Specialist
Research Contracts Branch
National Cancer Institute
Bethesda, Maryland 20014

Dear Mr. Benton:

This is in response to your letter concerning the funding for the Breast Cancer Detection Demonstration Projects.

The Board of Directors of the American Cancer Society has approved the recommendation of the Breast Cancer Task Force that the Society provide $50,000 for the first 20 projects during the third, fourth, and fifth year of operation, and $25,000 for the third, fourth, and fifth year of operation for the last seven. The budget for fiscal 1975-'76 was approved on this basis, and the budgets for 1976-'77, 1977-'78, and 1978-'79 will reflect this plan for funding.

You are correct in that sixth year funding for the 27 projects has not been discussed. The sixth year funding will be reflected starting with our 1977-'78 budget, and I will attempt to get a commitment at the May, 1976 meeting of our Board. I am certain that I will be asked for an estimate of the average operating cost per project for the sixth year, which should involve, for the most part, the fifth re-screen of the second five thousand women and their recalls. I expect there may be some unfinished business for the first five thousand but this should be a small item. Any cost estimates you may have prepared will be helpful.

Sincerely yours,

William M. Markel, M.D.

cc: Dr. Holleb
Dr. Pomerance
Dr. Byrd
Agnes Dixon

Copy to R. C. Cumming

"D"

August 1, 1975

Mr. John Dibeler
American Cancer Society
Long Island Division
535 Broad Hollow Road
Melville, New York 11746

Dear Mr. Dibelor:

In response to your telephone call today I enclose three copies of the reprint on the possible increase in breast cancer from x-ray mammography. This study estimates 10 screening examinations per subject at 1 rad absorbed radiation dose (5 rad skin dose) per mammogram, and calculates that this may increase the incidence of breast cancer by 2 percent. We believe that this estimate is a satisfactory one. We agree with the authors that the hazard of radiation is insignificant compared with the improvement in survival from early detection of the disease. Nonetheless we would like to reduce even this small added problem, and hope to foster methods to reduce the x-ray dosage by better equipment and also by considering an interval of screening of longer than one year.

In the American Cancer Society - National Cancer Institute demonstration projects the total cost per individual screening (physical exam, thermography, mammography, follow-up and administration) is about $20. In terms of cancers found the cost is vastly higher, of course, being something of the order of $6,000, but this is beside the point. The cancers detected in the projects are much smaller, and the fraction of patients free of axillary node metastases is nearly twice that in women seeking care themselves. Since 5 year survival with present treatment is almost twice as high with negative nodes, than with positive, we believe screening makes a major contribution to the breast cancer problem.

Although the American Cancer Society - National Cancer Institute projects have not yet reached a desirable proportion of minority groups, at least one project, that in Los Angeles, has in fact been able to do so. We think this proves it can be done, and are encouraging the others to work harder at this problem.

I shall show this letter to Bill Pomerance when he returns on Tuesday, August 5, and tell him to expect your call.

Sincerely yours,

Irvin C. Plough, M.D.
Associate Director for Program Planning
Division of Cancer Biology and Diagnosis
National Cancer Institute

~~File the correspondence~~

8/1/75

Dr Pencivance

Call today from Mr John Dibeler, ACS-Long Island Division.

He hopes to meet next week with the Gov. of N.Y. (or staff?) to convince him to sign a bill to fund some breast cancer detection units in NY state.

Dibeler wants information to counteract 3 criticisms raised about the ACS-NCI units. (Dibeler has talked in detail with Strax.)

1. Our units have not been very effective in reaching minority + low income groups.
2. Cost benefit – i.e. what is the cost per case detected?
3. Major problem: Radiation exposure.

I talked at length, and sent him the attached, enclosing copies of the Guthrie Clinic paper. Although this may help with his hope to get some NCI support for the NY program, he plans to call you for more information, and perhaps a more substantial letter, then.

BEST COPY AVAILABLE

AB

JUN 11 REC'D

AMERICAN CANCER SOCIETY-NATIONAL CANCER INSTITUTE
BREAST CANCER DEMONSTRATION PROJECTS

MEMO

May, 1975

1. It is two years since the first of the 27 breast cancer projects began operation (in 29 sites) with a goal of screening 140,000 women in the first year and an additional 140,000 women in the second year and following 280,000 women for a total of five years of screening and an additional five years of follow-up. Screening began in April, 1973, and gradually all 27 projects have become operational. As of January, 1975, approximately 125,000 women had been examined and breast cancers have been found at a rate of about 8.8 per 1,000 women examined (note, this figure is not precise). This is a creditable prevalence rate (i.e., number of cancers found at first screening) considering that this is a self-selected group and the incidence rate (number of cancers found on subsequent screenings) will probably be considerably less than this figure.

Many of the projects have had site visits after (over) 15 months of operation. All of the projects visited are examining adequate numbers of screenees and are finding an expected and acceptable number of cancers. Recommendations for biopsy range from few to many per cancer found and it is hoped that the significance of the numbers of biopsies necessary to find the most cancers will be determined by these projects (i.e., will projects recommending 10 biopsies per cancer find more or less cancers than those recommending 3 biopsies for each cancer found). Almost all of the projects are making extensive use of American Cancer Society volunteers; some can improve in this area.

Some of the problems found by the site visitors will be discussed.

2. Site visitors felt that the project pathologists have not been involved sufficiently in the projects. Lack of forms, improper indoctrination and other factors may have been the reason for this but it must be emphasized that when a lesion is identified and a biopsy advised, it is the responsibility of the project director to see that the project pathologist and the screenee's physician of record are notified, and the surgeon identified. In addition, the project pathologist and mammographer should make themselves aware as to where and when the biopsy is to be done (especially, if it is not done in the project hospital) and the mammographer should offer his services to the local pathologist in order to make more certain that he obtains the materials and information that will permit him to fill out the forms properly and more importantly, that the suspicious area in the mammogram is removed. It is vital to the success of the projects that the pathologist, mammographer and surgeon all cooperate in demonstrating to their community the necessity of specimen radiography, histological classification of the lesion, extent of axillary metastasis and other features indicated in the forms.

The project pathologist is expected to ask his counterpart in the treating hospital to submit gross specimens, if possible, as well as microscopic slides and tissue blocks of both benign and malignant lesions. Geographic or other situations may not make this always possible but a real attempt should be made to obtain this material as well as accurate reports.

The project information states; "When biopsy is recommended on radiologic evidence only, it should be determined by specimen radiography (see appendix) that the lesion identified radiographically has been removed by the surgeon." There will be some cases with physical findings in one area when the radiologist is suspicious of an area in another part of the breast or adjacent to the benign lesion and therefore there should be consultation for lesions of this sort and the responsibility of determining if such exists, rests with the project director and indirectly with the project pathologist.

These projects have been designed as "demonstration" projects with the best personnel that can be secured to demonstrate that screening and mammography will find small and occult breast cancers. The demonstration should extend to all physicians in the areas around the projects. Such educational objectives can be attained by project radiologists, pathologists and surgeons speaking periodically at respective meetings of members of their specialty and not only indicating what procedures are necessary for finding occult breast cancer but also reporting the projects' results, such as the fact that about 90 percent of these cases can be suspected or diagnosed by mammography and that only 20-25 percent of all cases found have axillary metastasis as compared to 50-60 percent of those women with symptomatic palpable lumps. The cooperation of all of these specialists is essential if these projects are to succeed.

3. In the project information, it should be noted that on page 8, option 2 and page 9 paragraph 2, a change has been made. If a screenee is noted to have only a positive thermogram, she will be rescreened at the discretion of the project director and not arbitrarily at 6 months as stated.

4. From the site visitors' reports it was not apparent that all project directors understood their responsibility to follow every woman entered in the projects for 10 years or to her death, and to find the cause of death, regardless of whether or not she returned for rescreening. This follow-up can be done through the screenee, if she is willing, the referring or doctor of record or through friends she has indicated on the identification sheet. Such information is most important for the statistical evaluation of the work done in these projects. It is believed that the American Cancer Society volunteers can be most helpful in locating women who might have been dissatisfied, recalcitrant or moved to other areas. Follow-up forms are being developed and will be distributed; these will be used in reporting on screenees who have not returned for rescreening. Similarly, an interval cancer report form is being developed that will be used to indicate the occurrence of cancer detected independent of the screen.

5. Again the importance of obtaining initial, independent readings, findings and reports of each examination is emphasized. Whether it is a physician, paramedic or technician, the initial reading form should be completed and the type of person making the report indicated. Later changes in screenee management can be made based on consultations, double readings, reports of other examinations and its conclusions never altered. It is important that the persons doing and reporting the initial examination should do so without any knowledge of the other examinations, i.e., one person read the mammograms, another the thermogram and another record the physical examinations. It is acceptable, if it is necessary because of inadequate numbers of personnel, for the same person to read the thermograms, for example, and later read the mammograms providing there is no identification of screenees.

The purpose of this separation of readings is to determine the role of each of these modalities of examination in the final determination of what is to be done. After each of these examinations is recorded independently, it is desired and indeed expected that a physician will review all three modalities as reported and then possibly recall or reexamine the screenee so that the best possible decision for that person can be made. Under no circumstances should the original report be altered but the final report will be based on all three modalities and perhaps even a reexamination of these. Fill out the initial form as you believe it should be filled out at that time and then call for help if you are uncertain! But don't change the original report after you call for help.

6. The recent workshop on thermography indicated that most of the thermograms were fair and some were good. There were a few that were not as good and probably should not have been read. There is definite room for improvement. The reasons for decisions based on thermography were discussed and it is recognized that better and more precise definitions for stating that a thermogram is positive or abnormal are needed and these definitions might well be established from these projects. It is generally accepted that no decision to biopsy a breast should be made on thermographic evidence alone. In these projects it is mandatory that there be more evidence than a positive thermogram. It is a "non-invasive" method of examination and perhaps some way can be found to reduce the frequency of x-ray exposure by using periodic thermography; but this method is not evident now.

7. We are interested in updating our list of ancillary projects that each of you may be involved in. We would appreciate receiving a list of these efforts and, if you have not given us a detailed description of any of these before, such complete information is desired. We would like to remind you that if these involve the screenees in any way, notification of the National Cancer Institute is required in advance of venturing into this area.

8. Bilateral Mastectomy Patients. Questions have been coming in as to the disposition of bilateral mastectomy patients. It is necessary to maintain contact with the patient on a regular basis so as to be aware of her status.

She of course should be followed by her surgeon or internist or family practitioner of record. The project should not assume responsibility for her medical observations.

9. There was some misunderstanding at the February 24, 1975, Bethesda meeting concerning the comprehensive history being prepared for the Case Control study. The project will have no responsibility for filling out these forms: they will be completed by trained interviewers under the supervision of the National Cancer Institute.

10. It is the goal of these projects to demonstrate that the best and most accurate method of detecting breast cancer can be applied to large groups of women. The ultimate goal is to have these, believed to be effective, methods recognized and adopted by the general health care system. Quality control is of the utmost importance and such control has already been established in mammography and thermography and similar control methods are being established for physical examination and pathology. The great dedication and excellence of all of the personnel in these projects is appreciated and apparent. Continuous monitoring of these projects is essential in order to be corrective and helpful at the earliest opportunity.

William Markel, M.D.
Project Officer
American Cancer Society
219 East 42nd Street
New York, New York 10017

William Pomerance, M.D.
Project Officer
National Cancer Institute
Building 31, Room 3A10
Bethesda, Maryland 20014

(301)496-1591

AMERICAN CANCER SOCIETY, INC.
219 EAST 42ND STREET • NEW YORK, N.Y. 10017 • (212) 867-3700

WILLIAM M. MARKEL, M.D.
VICE PRESIDENT FOR SERVICE
AND REHABILITATION

RESEARCH
EDUCATION
SERVICE

April 1, 1974

Mr. John P. Campbell, Jr.
National Cancer Institute
National Institutes of Health
Blair Building - Room 7A07
Bethesda, Maryland 20014

Dear Mr. Campbell:

The Board of Directors of the American Cancer Society approved the following recommendation at the meeting on February 8, 1974:

"That the following additional seven breast cancer detection demonstration projects be approved for funding in the amount of $25,000 per year per project for two years:

✓ Vanderbilt University (John R. Amberg, M.D.) (Henry Burko, M.D.) Nashville, Tennessee

✓ University of Arizona - Arizona Medical Center (C.D. Christian, M.D., Ph.D.) Tucson, Arizona

✓ St. Joseph Hospital (Duncan L. Moore, M.D.) Houston, Texas

✓ Rhode Island Department of Health (Herbert P. Constantine, M.D.) Providence, Rhode Island

Good Samaritan Hospital and Medical Center (Morton J. Goodman, M.D.) Portland, Oregon

✓ University of Southern California (Lewis W. Guiss, M.D.) Los Angeles, California

✓ Cancer Research Center (William L. Donegan, M.D.) Columbia, Missouri

We have been advised that the National Cancer Institute is prepared to fund these additional projects with limited funding from the American Cancer Society. This would bring the total number of breast cancer detection demonstration projects to 27."

Sincerely yours,

William M. Markel, M.D.

State University of New York at Buffalo

DR. MARVIN ZELEN, Director
STATISTICAL LABORATORY

FACULTY OF NATURAL SCIENCES AND MATHEMATIC

Hand Jan 9, 1974 meeting

MEMORANDUM

TO: Participants of January 9, 1974 meeting on Cancer Control: Breast Cancer Demonstration Projects

FROM: M. Zelen, Ph.D., Director
Statistical Laboratory, State University of New York at Buffalo

DATE: December 27, 1973

Other commitments prevent me from attending the meeting today. However, I wish to bring to your attention three documents which may be of interest to you. These are labeled A, B, and C and are attached. A and B were written early in 1973 after making several site visits for the Demonstration Project. C was presented a few weeks ago at a meeting called "Creative Concepts in Radiology", held in Colorado.

Briefly A contains a suggestion to alter the basic plan of the Demonstration Project so that it is a study which generates useful information and at the same time is enlarged to screen for cervical cancer. As most of you know, the benefits from cervical smears is open to question by virtue of the British Columbia Study (Aluwalia, H.S. and Doll, R. Mortality from cancer of the cervix uteri in British Columbia and other parts of Canada, Brit. J. Prev. Soc. Med. 22, 161 (1968). This Demonstration Project is a "golden" opportunity to obtain prospective data on the benefits of Pap Smears. At the same time it will help evaluate, in an unambiguous way, the benefits of early detection through mass breast screening. Recently I attended a meeting where a participant in the Demonstration Project was reporting 15-20 cases found per thousand. This is far above the HIP experience. Without a control group, we have no way of knowing whether these women are being helped or are simply being observed a longer time with disease.

B was written so that the subtleties associated with the evaluation of early detection screening programs are understood by clinicians and radiologists. Since writing this critique of the HIP program, I have learned that those individuals in the Study (screened) Group who failed to come in for an examination had significantly lower incidence (20 percent lower) of breast cancer than the control group. This makes the comment of section 5 even more pertinent.

C is self-explanatory and indicates that if the main object of the Demonstration Project is to diagnose more women with breast cancer early, there is a cheaper way of doing it. Note that at a prevalence rate of 2 per 1,000, the cost is $22-28 thousand dollars per case found for mammography. Even if the cost was reduced by a factor of 10 it would still be too expensive to be used as a mass public health measure. It should be used only in a screening program for high risk or suspicious individuals.

BEST COPY AVAILABLE

File
RB 11/2

AMERICAN CANCER SOCIETY, INC.
219 EAST 42ND STREET • NEW YORK, N.Y. 10017 • (212) 867-3700

ARTHUR I. HOLLEB, M.D.
SENIOR VICE PRESIDENT
FOR MEDICAL AFFAIRS
AND RESEARCH

RESEARCH
EDUCATION
SERVICE

CONFIDENTIAL

October 3, 1973

Dr. Nathaniel I. Berlin, Director
Division of Cancer Biology & Diagnosis
National Cancer Institute
Bethesda, Maryland 20014

Dear Nat:

I have not responded to your letter of July 31, 1973 about the Breast Cancer Detection Demonstration Projects because we have no record of having received it until now.

Now that I have read the criticisms, I do not feel qualified to answer with statistical expertise. It is my impression that had this same approach been used in the early 1950's, the Pap smear would not be in existence today, nor would there be a 60% reduction in the mortality from cervical cancer.

Nevertheless,

1. I suspect that the critic has had little or no experience with the clinical diagnosis and management of breast cancer. Will there never be an end to the "biological determinists" and "therapeutic nihilists" who minimize the importance of early diagnosis and prompt treatment, yet rush their wives to the physician's office at the first suspicion of possible cancer?

2. How can a statistician (who obviously needs time in the Breast Clinic of Memorial or M. D. Anderson) attach any significance to his own statement - "early detection case findings tends to detect cases which have longer pre-clinical durations"? What does all this mean? What is the meaning of "tends"? What is "pre-clinical" - lobular carcinoma in situ, a small palpable mass of invasive cancer, a mass too small to palpate? Who can tell how long a "pre-clinical" situation has existed? The critic draws diagrams which are pure hypotheses and meaningless clinically, yet presented as statistical gospel. This is a fine example of the application of statistical methodology without knowledge of the natural history of a disease process.

BEST COPY AVAILABLE

3. Yes, we will be able to answer many questions vitally important to clinicians without the recommended control group. For example, what is the value of thermography in relation to mammography and clinical examination, what is the value of all three techniques in relation to each other, what is the significance of the family history in the group studied, how many early cancers are found in the population screened and what happens to these patients, etc., etc.? I could go on and on.

4. The tubular vision of the critic does not see the broader implications of professional and public education in reducing the mortality of the #1 cancer killer of women.

5. Let's wait and see what age groups do come in and what the detection rate is. Is it less important to find minimal breast cancer in a woman 40 years of age than 60? Peter Medawar, in a recent editorial on the Cost/Benefit Analysis of Pure Research, referred to Oscar Wilde's definition of a cynic as "a man who knows the price of everything and the value of nothing."

6. We considered the possibility of including a Pap test and rejected it because breast cancer is the main target and because it is impractical considering the number of women being examined in short periods of time. Does the critic know what is entailed in doing a Pap test? The physical aspects of further undressing, an examining table, stirrups, etc. Why not also include a bimanual pelvic exam, a digital-rectal, an abdominal exam, etc.? The project could be extended to a complete physical examination, thoroughly computerized, but this is neither the message nor the focus of the program.

7. I don't need a "hypothetical case", nor do I need a theoretical diagram for breast cancer. Anyone who has treated this disease for twenty five years knows that Stage I breast cancer almost invariably does better than more advanced disease when treated surgically. One can't begin with a presumptive diagram and use the word "always" (see paragraph #3, page 2).

8. What does the critic mean by "slow growing disease"? Has anyone ever proved that "slow growing disease" has "fewer patients with axillary nodal involvement"? What do we have to do to prove that early detection is "beneficial"?

9. The critic (page 6) obviously doesn't understand the potential role of mammography and the possible saving of lives when mammography is combined with thermography and clinical examination. To anticipate that the physical examination which discovers a readily palpable cancer may benefit a patient more than a mammogram which discovers a nonpalpable in situ cancer proves a lack of understanding about clinical breast cancer.

10. I respect the judgment of well versed statisticians and often call upon them for advice. However, there is a limit for statistical application to all avenues of medicine. Many good statisticians recognize the value of sound medical practice, good patient care, public education, professional education and cancer control. One could further minimize the breast projects by now insisting on an animal model system before we examine the first patient. In the meanwhile, more women die needlessly of breast cancer.

11. Sure, maybe the Pap smear doesn't account for all the reduction in mortality from cervical cancer (more hysterectomies, declining incidence). But, doesn't all this become an exercise in statistical futility when the Pap smear is simply good medical practice for the patient of today who may have early cancer of the cervix undetected visually? Perhaps mammography, thermography and well done clinical examinations will become the equivalent for breast cancer. Let's try to find out practically - not by theoretical diagrams which simplistically refer to a "duration of pre-clinical disease" without any true concept of evaluation or meaning.

12. Lastly, I am always suspect of the man who comments on a breast cancer project and often refers to the anatomic site as the "brest".

Sincerely,

Art

Arthur I. Holleb, M.D.

To Dr. Masnyk
June 1980

BREAST CANCER DETECTION CLINIC
911 Seneca
Seattle, Washington 98101

September 6 - December 31, 1973

1831 Women Screened

35 Biopsies Recommended

- 12 Cancers
  - 10 Negative Nodes
  - 2 Positive Nodes
- 15 Benign
- 8 Not Yet Determined

Participating Hospitals

Burien General	1
Doctors Hospital	1
Group Health	6
Providence	1
Seattle General	1
Swedish	5
Tacoma General	1
U.S. Public Health Service	4
Virginia Mason	9
Valley General	1
Waldo	1

SUMMARY OF THE TABLES

Demographic Data

Table 1	Reasons for Examination
Table 2	Source of Information on Program
Table 3	Race
Table 4	Religion
Table 5	Marital Status
Table 6	Family Income

Examination and History Data

Table 7	Examination Evaluations
Table 8	Data Entry Errata

(Totals may not crossfoot due to multiple responses and omissions)

TABLE 1

DEMOGRAPHIC DATA
"Reasons for Examination"
Based on Patient Histories Available

Project	(code)	No. Screened	Routine Checkup	Might have Breast Dis.	Might have Breast CA	Family His. Br. CA	Phy.	Other
Atlanta	03	7	6				1	
Boise	08	666	487	40	22	121	50	98
Cincinnati	11	80	65	4		4	3	6
Jacksonville	24	24	14	1		4	2	4
Philadelphia	13	153	75	11	1	21	7	41
Seattle	06	186	127	7	1	37	8	24
TOTALS		1,116	774	63	24	187	71	173

Note: These categories are not mutually exclusive; multiple answers are legitimate.

TABLE 2

DEMOGRAPHIC DATA
Source of Information on Program

Project	Number Screened	TV	Radio	Newspaper	Poster	Church	Mtg.	Friend	ACS	Phy.	Othe
Atlanta	7	1	1	3				3			
Boise	666	33	6	211	46	20	66	317	72	15	37
Cincinnati	80	3	1	41	1		3	16	7	5	8
Jacksonville	24	2		14				2	2	3	2
Philadelphia	153	21	2	103			2	14	3	4	6
Seattle	186	48	9	93		1	5	35	7	3	9
TOTALS	1,116	108	19	465	47	21	76	387	91	30	62

BEST COPY AVAILABLE

TABLE 3

DEMOGRAPHIC DATA
"RACE"

Project	Number Screened	Cauca. n/Span	Cauca Span.	Black n/Span	Black Span.	American Ind./Esk.	Jap.	Chin.	Other Orien.	Other	Unce
Atlanta	7	6		1							
Boise	666	651	6	1	1	1	4	1			
Cincinnati	80	69	7	3						1	
Jacksonville	24	22	1							1	
Philadelphia	153	132	8	10	2				1		
Seattle	186	172	6	2	1	1	1				
TOTALS	1,116	1052	28	17	4	2	5	1	1	2	

TABLE 4

DEMOGRAPHIC DATA
"Religion"

Project	Number Screened	Catholic	Jewish	Mormon	7th day Adventist	Protestant	Other	Uncer.	None
Atlanta	7		1			6			
Boise	666	83	4	89	4	444	26	3	13
Cincinnati	80	12	10			54	2		2
Jacksonville	24	3	2			18	1		
Philadelphia	153	49	52			38	2	3	5
Seattle	186	45	13	4	1	100	9	3	9
TOTALS	1,116	192	82	93	5	660	40	9	29

TABLE 5

DEMOGRAPHIC DATA
"Marital Status"

Project	Number Screened	Married	Single	Divorced	Separated	Widowed
Atlanta	7	5		1		1
Boise	666	505	20	63	8	65
Cincinnati	80	64	2	9		5
Jacksonville	24	19		2		3
Philadelphia	153	112	10	8	6	17
Seattle	186	140	3	20	2	21
TOTALS	1,116	845	35	103	16	112

TABLE 6

DEMOGRAPHIC DATA
"FAMILY INCOME"

Project	Number Screened	Under 5,000	5,000 9,999	10,000 14,999	15,000 29,999	30,000 99,999	100,000 up	Uncertain
Atlanta	7	1		4	2			
Boise	666	80	174	182	154	41		33
Cincinnati	80	7	19	16	21	11		6
Jacksonville	24	6	4	4	7	1		1
Philadelphia	153	18	37	32	36	12		9
Seattle	186	32	32	48	60	5	1	4
TOTALS	1,116	144	266	286	280	70	1	53

BEST COPY AVAILABLE

TABLE I

EXAMINATION EVALUATIONS OF SIX PROJECTS

(Based on data available to the Statistical Center as of 1/2/74)

			THERMOGRAM										
			Positive				Negative						
			MAMMOGRAM				MAMMOGRAM						
			Positive		Negative		Positive		Negative				
			PHYSICAL		PHYSICAL		PHYSICAL		PHYSICAL				
Projects	(code)	Number Screened	Pos.	Neg.	Pos.	Neg.	Pos.	Neg.	Pos.	Neg.	Biopsies Recommended	Biopsies Performed	Verified Cancers
Atlanta [1]	03	213	1	2	0	25	0	2	0	183	66		
Atlanta [1,2] (thermograms) omitted	03	909					23	29	2	855			
Boise	08	204	1	5	0	21	0	13	0	164	3		
Cincinnati	11	209	2	6	5	38	4	21	18	115	25		
Milwaukee [1]	05	2333	4	11	4	733	1	20	17	1543	57	40	11
Philadelphia	13	153	4	7	3	38	0	15	4	82	6		
Seattle	06	614	6	10	5	72	14	29	7	471	16		
TOTALS		3726	18	41	17	927	19	100	46	2558	173	40	11

[1] Totals were prepared by the Project.

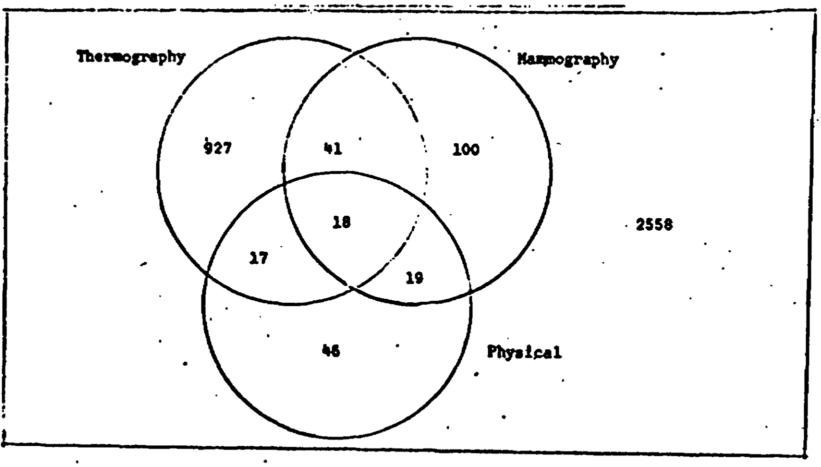
[2] Due to a failure of thermography equipment, a separate line is included for results of mammograms and physical examinations. This was done to present the data and isolate a problem. These figures are not included in the totals.

SUPPLEMENT TO TABLE 7 EXAMINATION EVALUATIONS

It is often difficult to readily visualize from a table the proper allocations of categories in three dimensional space. Some of this difficulty may be overcome by the use of a pictorial device called a Venn Diagram, which is familiar to most logicians. Such a figure is shown below with the appropriate values inserted from the table.

The three examinations Thermography, Mammography, and Physical are represented by circles. The area within an appropriate circle represents a positive reading, and the area exterior to the circle represents a negative one. The areas common to the circles then provide a representation of the desired breakdowns.

Venn Diagram of Examination Evaluations



CURRENT STATUS OF PROJECTS

Location	Office No.	Operational Date	No. Patients Screened	As of: (Date)
New York City	01	4/ /73	10,000	9/1/73
Atlanta (Emory)	02	7/1/73	440	12/19/73
Atlanta (Geo. Bapt.)	03	9/ /73	1,122	12/15/73
Louisville	04	8/ /73	1,900*	12/31/73
Milwaukee	05	7/1/73	2,333	12/12/73
Seattle	06	9/6/73	1,100*	12/15/73
Oklahoma City	07	11/1/73	3,000*	12/31/73
Boise	08	11/1/73	663	12/31/73
Newark	09	11/7/73	90	12/31/73
Kansas City	10	8/ /73	1,200*	12/31/73
Cincinnati	11	7/ /73	2,000*	1/1/74
Jacksonville	12	12/17/73	24	12/31/73
Philadelphia (Einstein)	13	12/1/73	153	12/28/73
Philadelphia (Temple)	14	2/ /74		
Pittsburgh	15	5/ /74		
Wilmington	16	2/1/74		
Ann Arbor	17	'74		
Des Moines	18	4/ /74		
Honolulu	19	2/1/74		
Oakland	20	2/1/74		
Washington, D.C.	21	—		
Durham	22	1/ /74		

*Estimated

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

NATIONAL CANCER INSTITUTE

August 9, 1973

Nathaniel I. Berlin, M.D.
Director, Division of Cancer
Biology and Diagnosis
National Cancer Institute
Building 31, Room 3A03
Bethesda, Maryland 20014

SUBJECT: Breast Cancer Demonstration Projects - Jointly Sponsored by the American Cancer Society and National Cancer Institute

Dear Doctor Berlin:

OVERALL PROJECT SUPERVISORS

Arthur Holleb, M.D.
American Cancer Society
219 East 42nd Street
New York, New York 10021
(212) 867-3700

Nathaniel I. Berlin, M.D.
Director
Division of Cancer Biology and Diagnosis
National Cancer Institute
Building 31 Room 3A03
Bethesda, Maryland 20014
(301) 496-4345

John Bailar, M.D.
Acting Associate Director
Division of Cancer Control
National Cancer Institute
Building 31 Room 10A25
Bethesda, Maryland 20014
(301) 496-6317

PROJECT OFFICERS

Kenneth B. Olson, M.D.
National Cancer Institute

Mrs. Susan Ficker, Associate
National Cancer Institute

Ihor J. Masnyk, Ph.D., Associate
National Cancer Institute

William Markel, M.D.
American Cancer Society

NOTE: Dr. Markel has indicated that the actual operation of these projects will be by the National Cancer Institute, but regular forms will go to him as well as to Kenneth B. Olson, M.D. of the National Cancer Institute. The latter person will coordinate all activities and be a central focus for information, questions, difficulties, etc. The American Cancer Society as well as the National Cancer Institute will be informed of the success (or failure) of each project and cooperate in any final reports.

PROJECT DIRECTORS

Dr. Philip Strax
Guttman Institute
2 East 87th Street
New York, New York 10028
(212) 427-4433

Dr. R. Waldo Powell
Emory University
School of Medicine
1365 Clifton Road, N.W.
Atlanta, Georgia 30322
(404) 377-2472

Dr. Condict Moore
University of Louisville
627 S. Floyd Street
Louisville, Kentucky 40402
(502) 582-2111 ext. 510

Dr. James E. Youker
Professor and Chairman
The Medical College of Wisconsin
561 North 15th Street
Milwaukee, Wisconsin 53226
(414) 258-2080

Dr. Thomas Carlile
The Mason Clinic
1118 Ninth Avenue
Seattle, Washington 98101
(206) 623-3700

Dr. Joanne Haberman
University of Oklahoma Health Science Center
P.O. Box 26901
Oklahoma City, Oklahoma 73190
(405) 271-5134

Dr. Alfred M. Popma
Mountain States Tumor Institute
151 East Bannock
Boise, Idaho 83702
(208) 345-1780

Dr. Benjamin Rush
New Jersey College of Medicine and Dentistry
100 Bergen Street
Newark, New Jersey 07103
(201) 643-6431

Dr. Loren J. Humphrey
University of Kansas Medical Center
Department of Surgery
Rainbow Boulevard at 39th Street
Kansas City, Kansas 66103
(913) 831-6101

Dr. Marvin McClow
St. Vincent's Medical Center
Department of Radiology
Barrs Street and St. Johns Avenue
Jacksonville, Florida 32204
(904) 389-7751 ext. 8332

Dr. Myron Moskowitz
University of Cincinnati
College of Medicine
Eden and Bethesda Avenues
Cincinnati, Ohio 45219
(513) 872-4396

BEST COPY AVAILABLE

THIS IS THE FIRST OF A NUMBER OF NEWSLETTERS

A Statistical Center has been awarded to the University City Science Center of Philadelphia. Dr. John Kapp Clark or Mr. William C. Ellenbogen can be contacted at the University City Science Center, 3508 Science Center, Philadelphia, Pennsylvania 19104. The telephone number is (215) 387-2255, if anyone is concerned. They are still at work on forms, procedures, contacts and other elements of their functions and it might be well to wait until they have had a chance to organize their approach to the procedures. They may be in touch with you for information or other matters.

It is important to know that they have been employed for the following reasons:

1. To be helpful to all of the projects.
2. To provide some uniformity of procedure.
3. To gather data from each project as well as the project as a whole.
4. To provide periodic reports to the National Cancer Institute and the American Cancer Society.
5. To help projects that might be foundering and to retail information that may be valuable to other projects.

There are eleven projects that have been funded and are in stages of operation. It is anticipated that nine more projects will be selected at the September 12, 1973 meeting of the Diagnostic Research Advisory Group making a total of five projects in each of the four geographic areas delineated by the American Cancer Society. Namely, these are the South, Northeast, Midwest and and West. All of these areas have comparable populations in terms of numbers. Many good projects cannot be funded. About 54 centers have applied and twenty (20) will be selected. Selection is based first on competence in three areas: (1) Professional; (2) Organizational Support; (3) Rapport and Use of the Local Units of the American Cancer Society. The latter is quite important, but does not preclude the use of other organizations in the recruitment and follow-up of screenees.

There will be a meeting of all project directors on September 24, 1973 at the Sheraton Hotel, 17th and John F. Kennedy Boulevard, Philadelphia, Pennsylvania, (215) 568-3300 or 800-325-2525. This meeting will be of project directors or their designee only. There will be one representative from each project and this conference will discuss forms, procedures, trials, and most importantly, policies. There will be other later meetings of project coordinators, secretaries, technicians, etc., but this first meeting will be for project directors or their designee only. Costs of this trip should be from the project budget and no other travel costs or per diem will be provided unless it is planned and approved by the National Cancer Institute Project Officer (Kenneth B. Olson, M.D.) for good reason. Project directors whose contracts have not yet been funded will be furnished transportation and per diem costs if we are notified.

At this meeting (i.e., September 24, 1973) it is planned to have most of the preliminary forms in hand and to discuss them. In the meantime, those projects that have already started will collect information in their own format, but the content should be the same as in the project appendix.

Questions can be directed to:

Kenneth B. Olson, M.D.
Chief, Diagnosis Branch
Division of Cancer Biology and Diagnosis
National Cancer Institute
Building 31 Room 3A03
Bethesda, Maryland 20014
(301) 496-1591

Mrs. Susan Ficker
Cancer Control Program
National Cancer Institute
Building 31 Room 3A10
Bethesda, Maryland 20014
(301) 496-1673

Ihor J. Masnyk, Ph.D.
Division of Cancer Biology and Diagnosis
National Cancer Institute
Building 31 Room 3A04
Bethesda, Maryland 20014
(301) 496-1591

Sincerely yours,

Kenneth B. Olson, M.D.
Chief, Diagnosis Branch
Division of Cancer Biology
and Diagnosis
National Cancer Institute

PROFESSIONAL EDUCATION, SERVICE AND REHABILITATION SUGGESTIONS FOR NCI

1. Contract with the American Academy of Family Physicians to survey and evaluate the attitudinal approach to cancer of the family doctor who represents the first-line physician in earlier diagnosis of cancer.

   Budget - estimate $50,000

2. Major project to develop hard data on the cost benefit ratio of early vs. late diagnosis of cancer - financial aspects. There is too little information about the cost and hardships to U. S. citizens when cancer is discovered at a late stage or when the disease is virtually incurable. The loss of money and time, the family disruption, etc., should be itemized for anatomic site and totality.

   Budget - estimate $75,000

3. Expand number of Breast Cancer Demonstration Projects - possibly 10 more and extension of support to 5 years rather than 2 years. Cost sharing with ACS.

NOTE

   There are at least 10 more suitable programs which have been site visited and evaluated. The demand for these examinations already exceeds the capability of some ongoing projects. So far, this is the most visible of the NCI's cancer control programs.

   Budget - $2,000,000 per year

4. Demonstration projects on the use of mobile cancer detection units.

   The studies of Henry Lynch at Creighton University in Omaha have been reported in the journals Cancer and Geriatrics. All details are available about his experience with mobile detection units designed for rural areas. (Unit cost - $37,500 equipped, salaries $66,000, traveling costs $4,000 - plus a variable amount for consumable supplies.) The examination is comprehensive - pelvic, pap test, procto, mammogram, etc. - multiphasic approach. About 250 patients seen per month - cost per patient ranges around $25-$30 depending on sex of patient.

   This could be an excellent opportunity for the NCI to cooperate with ACS, local medical societies, health departments, etc.

   The purpose would be to demonstrate whether mobile units can be effective in disease detection, especially cancer, in rural areas of the U.S.

   A highly visible project to the public and certain Congressmen.

[illegible]

Steve Fisher
4/30/73
1:30

AMERICAN CANCER SOCIETY, INC.
219 EAST 42ND STREET • NEW YORK, N.Y. 10017 • (212) 867-3700
WILLIAM M. MARKEL, M.D.
VICE PRESIDENT FOR SERVICE
AND REHABILITATION

RESEARCH
EDUCATION
SERVICE

Kep

RECEIVED
APR 30 1973

April 27, 1973

Kenneth B. Olson, M.D.
Chief, Diagnosis Branch
Division of Cancer Biology and Diagnosis
National Cancer Institute
Building 31, Room 3A-06
Bethesda, Maryland 20014

Dear Ken:

Enclosed is a status report as of April 26th.

Pondville

Rhode Island

I plan to visit BCA #39 and #43 early in May. We will check with the Tennessee Division concerning BCA #49.

Applications exist for Category V, but they have not been sent to us and therefore they do not have BCA numbers.

Sincerely yours,

William M. Markel ej

William M. Markel, M.D.

Encl.
cc: Agnes Dixon

BEST COPY AVAILABLE

April 20, 1973

PROGRESS REPORT ON BREAST CANCER DEMONSTRATION PROJECT APPLICATIONS

I. Approved, contracts negotiated:

BCA #3 University of Louisville School of Medicine
Louisville, Kentucky
(Condict Moore, M.D.)
$284,290

BCA #5 Emory University School of Medicine
Atlanta, Georgia
(Douglas L. Buckner, M.H.A.)
$301,751

BCA #8 Stella and Charles Guttman Breast Diagnostic Institute, Inc.
New York, New York
(Philip Strax, M.D.)
$684,300

II. Approved, contracts being negotiated.

(HAVE ACS BOARD APPROVAL AS OF OCTOBER 1972)

BCA #2 St. Vincent's Medical Center
Jacksonville, Florida
(Marvin V. McClow, M.D.)
$238,703

BCA #6 Kansas University Medical Center
Kansas City, Kansas
(Loren V. Humphrey, M.D.)
$490,592

(REQUIRE ACS BOARD APPROVAL IN JUNE 1973)

BCA #9 University of Cincinnati
Cincinnati, Ohio
(Myron Moskowtiz, M.D.)
$804,123

BCA #12 Virginia Mason Hospital
Seattle, Washington
(Thomas Carlile, M.D.)
$442,908

BCA #19 College of Medicine and Dentistry of New Jersey
(Newark, New Jersey
(R.V.P. Hutter, M.D.)
$572,981

BCA #25 University of Oklahoma
(Oklahoma City, Oklahoma
(JoAnn D. Haberman, M.D.)
$514,695

BCA #28 Mountain State Tumor Institue
Boise, Idaho
(Dr. Alfred M. Popma)
$416,269

BEST COPY AVAILABLE

BCA #33	Medical College of Wisconsin Milwaukee, Wisconsin (James E. Youker, M.D.) $170,157

III. Deferred at April DRAG Meeting - To be resubmitted by August DRAG Meeting:

BCA #1	Georgetown University Washington, D.C. (Margaret Abernathy, M.D.) $268,643
BCA #4	The Johns Hopkins University School of Medicine Baltimore, Maryland (R. Robinson Baker, M.D.) $330,901
BCA #18	Vanderbilt University Nashville, Tennessee (John R. Amberg, M.D.) (Henry Burko, M.D.) $294,306
BCA #20 21	Temple University Health Sciences Center Philadelphia, Pennsylvania (Marc S. Lapayowker, M.D.) $208,249
BCA #22	Albert Einstein Medical Center Philadelphia, Pennsylvania (Harold J. Isard, M.D.) $284,238
BCA #24	Holy Cross Hospital Salt Lake City, Utah (Gerald P. Stevenson) $456,797
BCA #27	Regent's University of California Los Angeles, California (Richard H. Gold, M.D.) $443,365
BCA #29	University of Arizona, Arizona Medical Center Tucson, Arizona (C.D. Christian, M.D., Ph.D.) $305,406
BCA #31	Iowa Lutheran Hospital Des Moines, Iowa (Dr. Donald C. Young) $283,179

BCA #32	St. Joseph Hospital Houston, Texas (Duncan L. Moore, M.D.) $500,807.50
BCA #34	Wilmington Medical Center Wilmington, Delaware (Leslie W. Whitney, M.D.) $311,869
BCA #35	Lester E. Cox Medical Center Springfield, Missouri (Carl T. Rinker, M.D.) $205,652.32

IV. Will have been ACS/NCI Site Visited for action at August DRAG Meeting:

BCA #11	Jamaica Hospital Jamaica, New York (Dr. Jugh J. Barber)	Revised application sent to NCI 3/14/73 site visited by Dr. Markel
BCA #17	Mount Sinai Medical Center Miami Beach, Florida (Dr. J.B. Cunningham) $325,500	Sent to NCI 4/10/73
BCA #30	Orange County Medical Center Orange, California (Dr. Lawrence Brown) $199,173	Sent to NCI - 3/8/73
BCA #36	Straub Medical Research Institute, Inc. Honolulu, Hawaii (Dr. Fred Gilbert, Jr.) $400,917	Sent to NCI - 2/21/73
BCA #37	Wyckoff Heights Hospital Brooklyn, New York (Dr. Philip A. Zoller) $180,090	Sent to NCI - 4/17/73
BCA #38	Duke University Medical Center Durham, North Carolina (Dr. Richard C. Lester) $323,330	Sent to NCI - 3/8/73
BCA #39	Rhode Island Department of Health Providence, Rhode Island (Dr. Herbert P. Constantine) $399,800	Dr. Markel to Site Visit

BCA #40	Regional Health Resource Center Urbana, Illinois (Dr. Ben T. Williams) $415,770	Sent to NCI - 3/8/73
BCA #41	Baylor University Medical Center Dallas, Texas (Dr. A. D. Sears)	Sent to NCI - 3/14/73
BCA #42	University of Pittsburg Pittsburg, Pennsylvania (Dr. Bernard Fisher)	Sent to NCI - 4/17
BCA #43	Faulkner Hospital Pondville Hospital Walpole, Massachusetts (Drs. Sadovsky & Messer)	Dr. Markel to Site Visit
BCA #44	Samuel Merrit Hospital Oakland, California (Dr. Robert Schweitzer)	Sent to NCI - 3/30/73
BCA #45	University of California San Francisco (Dr. Granville C. Coggs)	Sent to NCI - 3/30/73
BCA #46	Mayo Foundation Rochester, Minnesota (Dr. John J. Gisvold)	Sent to NCI - 3/28/73
BCA #47	Green Cross General Hospital Cuyahoga Falls, Ohio (William H. Voorheis, D.O.)	Sent to NCI - 3/15/73
BCA #48	Bio Products, Inc. Oxon Hill, Maryland 20021 (Donald L. Price, Ph.D.)	Sent to NCI - 3/26/73
BCA #49	Meharry Medical College Nashville, Tennessee (Dr. Gadson J. Tarleton)	Awaiting Division Approval
BCA #50	Midtown Hospital Association Denver, Colorado (Dr. Freeman H. Longwell) $568,335	Sent to NCI - 3/22/73
BCA #51	Good Samaritan Hospital and Medical Center Portland, Oregon (Dr. Morton J. Goodman) $448,734	Sent to NCI -3/22/73

BCA #52 Creighton University School of Medicine — Sent to NCI - 3/2273
Omaha, Nebraska
(Dr. Henry T. Lynch)
$407,935

BCA #53 University of Southern California — Sent to NCI - 3/30/73
Los Angeles, California
(Dr. Lewis W. Guiss)

V. Applications expected for consideration at August DRAG Meeting:

Cancer Research Center
Columbia, Missouri
(Dr. William L. Donegan)

University of Michigan
University Hospital
Ann Arbor, Michigan
(Dr. Walter M. Whitehouse)

Roswell Park Memorial Institute
Buffalo, New York
(Dr. Thomas L. Dao)

VI. Applications disapproved at April 19 DRAG Meeting:

BCA #7 University of Virginia School of Medicine
Charlottesville, Virginia
(Dr. Theodore E. Keats)
$152,346

BCA #13 Kerry Medical Foundation
Ann Arbor, Michigan
(Dr. Robert L. Kerry)
$280,316

BCA #14 Methodist Hospital of Gary Indiana
Gary, Indiana
(Dr. Gerald Thomas)
$254,218

BCA #23 Good Samaritan Hospital
Phoenix, Arizona
(Dr. Theodore Ditchek)
$340,267

BCA #26 Children's Hospital of San Francisco
San Francisco, California
(Dr. Victor Richards)
$1,111,399

SUMMARY SHEET

SEE ITEM J, P. 4

1. GENERAL INFORMATION

A.	This proposal is for a new contract.	
B.	Name of Contractors:	See Attachment A
C.	Address of Proposed Contractors:	See Attachment A
D.	Project Title:	Breast Cancer Detection Demonstration Project
E.	Program Area:	Cancer Control
F.	Project Officer:	Dr. Kenneth B. Olson
	Assistant Project Officer:	Ms. Susan J. Ficker
G.	Identity of Review Bodies:	Initial: Cancer Control Advisory Committe Final : Diagnostic Research Advisory Gro
H.	Contractor's Principal Investigator:	See Attachment A
I.	Contractor's Co-Principal Investigator:	------
J.	Approval Information:	

1. /s/ Kenneth B. Olson	Project Officer	5/1/73 Date
2. /s/	Deputy Associate Director for Cancer Control	5-2-73 Date
3. /s/	Contracting Officer RCB, OD, NCI	5/2/73 Date

II. FISCAL INFORMATION

A. Desired starting date for new contract and proposed period it is to cover:

July 1, 1973 -- Twelve (12) months

B. Estimated number of renewals required beyond first year:

Six (6)

C. Estimated Cost (Recommended by Program Area)

1. Estimated Cost per contract of initial period:

   $200,000

2. Estimated Cost per contract of first renewal:

   $200,000

3. Estimated Cost per contract of last five (5) renewals:

   $40,000

4. Estimated Cost per project of all years:

   $600,000

III. Project Information

A. A description of the project and its objectives:

The Contractor will perform breast cancer detection screenings of a specified number of women to demonstrate the effectiveness of current techniques. It is hoped that this project will confirm the observation that non-palpable breast cancer, promptly treated, will provide more years free of known disease than would have been expected for women with palpable tumors. This project will require the ability to recruit sufficient numbers of asymptomatic women for screening. There must be a close liaison with the local chapter of the American Cancer Society, since the ACS volunteers will be instrumental in assuring an effective project.

B. Contractor's qualifications:

A list of the qualifications necessary for a successful project is contained in Attachment B. All proposals forwarded to NCI from ACS, co-sponsor of the project, have guaranteed financial support of the National ACS and the publicity services and volunteer support of the local ACS chapter.

1. College of Medicine and Dentistry in Newark has a superbly organized program with the full cooperation of the University administration and the medical community. The American Cancer Society presented a detailed plan of recruitment of women from the area surrounding the medical center which is largely populated by minority groups. The radiologist involved in the project has had excellent experience in mammography.

2. St. Vincent's Medical Center showed the technical expertise necessary for performance in this contract. They have the ability to recruit women to the screening program and they have the administrative capabilities to organize and maintain a successful screening program.

3. The Medical College of Wisconsin has had considerable experience in mammography and thermography. The Project design has been well organized and adequate recruitment and follow-up of screenees is assured.

4. The University of Cincinnati has the adminstrative capabilities to initiate and maintain a successful screening project. The technical staff is experienced and fully qualified.

5. Kansas University Medical Center has an experienced professional staff with expertise in both the technical and administrative areas. They have the firm support of the local medical and community groups as well as the American Cancer Society and this will ensure proper patient accrual and follow-up.

6. Virginia Mason Hospital has been a leader in the field of mammography. Their professional staff is well organized to operate an efficient breast cancer screening project.

7. Mountain States Tumor Institute has an exceptionally well organized project with the full support of the local medical society and community service organizations as well as the American Cancer Society. It is uniquely qualified to recruit and follow-up a sufficient number of women. The professional staff possesses the necessary technical skills for performance of this contract.

8. The University of Oklahoma has the adminstrative capabilities to efficiently operate a breast cancer screening project. The Project Director is experienced in mammography and has been instrumental in the development of thermography.

C. Twenty-four proposals were recommended to the NCI. These offerors were reviewed and jointly site visited by the NCI and ACS. Sixteen of the institutions which were reviewed were considered to lack the necessary qualifications for this project. (See Attachment C.)

D. Other related project against which proposed effort was checked:

There are no other efforts which duplicate or conflict with this project.

BEST COPY AVAILABLE

E. **Project initiated by:**

NCI Staff

F. **Site Visits:**

Formal site visits were performed jointly by the NCI and ACS. See Reports Attached.

G. **Relationship to Total Program:**

The Cancer Control Program has, as one of its objectives, the widespread demonstration of new cancer control knowledge, processes and skills to health professionals and to the general public. The purpose of this procurement is to provide for the demonstration of early breast cancer detection screening. Of prime concern too, is the control of cancer with a view toward obtaining maximum reduction in cancer mortality, incidence and disability. By providing for the early detection and diagnosis of breast lesions, the proposed demonstration projects will be of much significance in the control of cancer of the breast.

H. **Contract vs. Grant Mechanism:**

This project is a non-research effort to accomplish widespread application of the latest available knowledge of breast cancer detection screening in accordance with NCI requirements. There is no capability within NCI to perform an effort of this nature. A central statistical group will be compiling all result data for report and planning purposes. Accordingly, the project must provide meaningful results within a limited time period. Only through the contract mechanism can the necessary direction and control be provided to obtain the maximum return from this project in terms of the Program objectives.

J. **Review Channels:**

The local chapters of the ACS publicized the projects, reviewed proposals on a competitive basis, and performed initial site visits, and the applications were reviewed by the national office of the ACS. The proposals which were approved were site visited jointly by ACS and NCI and final recommendations were brought before the Diagnostic Research Advisory group. The eight subject proposals were approved for funding.

BEST COPY AVAILABLE

AMERICAN CANCER SOCIETY, INC.
219 EAST 42ND STREET · NEW YORK, N.Y. 10017 · (212) 867-3700
ARTHUR I. HOLLEB, M.D.
SENIOR VICE PRESIDENT
FOR MEDICAL AFFAIRS
AND RESEARCH

RESEARCH
EDUCATION
SERVICE

October 20, 1972 File

Dr. Nathaniel Berlin
Director
Division of Cancer Biology & Diagnosis
National Cancer Institute
Bethesda, Maryland 20014

[illegible]

Dear Nat:

Enclosed is a draft of the notes made at our meeting on October 16th. I did not get an opportunity to discuss them with John when I was in Washington on Wednesday.

Please let me know if there are any revisions.

We will be in touch with John as soon as the Task Force Committee meets.

Best personal regards.

Sincerely,

Art

Arthur I. Holleb, M.D.

[illegible]

cc: John C. Bailar, III, M.D.
Mr. Hugh Mahanes
Sidney L. Arje, M.D.
William M. Markel, M.D.
Mrs. Jeanne Weddle
Mr. Alan Davis
Mr. Richard McGrail

BEST COPY AVAILABLE

SEE item 1,
4th-to-last page

Statement

of

Arthur I. Holleb, M.D.

Senior Vice President for Research
and Medical Affairs

AMERICAN CANCER SOCIETY

before the

United States House of Representatives

92nd Congress

Committee on Appropriations

Subcommittee for Labor, Health, Education and Welfare

for FY 1973

May 3, 1972

BEST COPY AVAILABLE

Mr. Chairman and Members of the Committee:

I am Dr. Arthur I. Holleb, Senior Vice President for Medical Affairs and Research, of the American Cancer Society. I am a surgeon, and serve as the Chief Medical Officer of the American Cancer Society, and am administratively responsible for the Society's programs in professional education, service to the patient - including rehabilitation programs, and research. I have served in this capacity with the American Cancer Society since 1968, and prior to that I was a member of the Surgery Departments and Associate Director at the University of Texas, M.D. Anderson Hospital and Tumor Institute at Houston, and the Memorial Sloan-Kettering Cancer Center in New York City.

I am here to present the position of the American Cancer Society on the funding for Fiscal Year 1973 of Cancer Control -- that element of the dynamic new cancer program that stands out as the critical mass denoting the change in direction of the National Cancer Institute from its former research-only mission, to the new synergistic concept encompassing all aspects of man's scientific attack on cancer.

One of the tragedies and travesties of our modern age of technological progress is that huge barrier between the development of a new advance against cancer, and getting it to the people with the disease. Cancer Control programs will serve to break down that barrier.

Dr. A. Hamblin Letton, current President of the American Cancer Society, stated recently at the Society's annual Science Writers' Seminar that two-thirds of the victims of cancer could be saved today if present knowledge were effectively applied. He added,

> "Most authorities agree now that if all we know about cancer could be applied through mass screening, early detection, the best surgery, the most effective radiation therapy, and selected chemotherapy, the potential cure rate might well be better than two thirds, instead of half."

In cancer, we are dealing with what is essentially a curable disease, and one that is, in many cases preventable. In both cure and prevention, however, we are regretably behind in applying, and practicing what is possible, as Dr. Lotton has stated: The patient of today needs what is possible now. He cannot wait for the unpredictable results of research in the future.

Through an aggressive cancer control program, the National Cancer Institute, with coordination, collaboration, and cooperative effort of the private sector represented principally by the American Cancer Society, could realize, in a relatively short period of time, a much higher application of existing knowledge of cure, prevention, and rehabilitation of cancer patients throughout the country.

Cancer control is the element of the National Cancer Program that will be directly visible to all of the people -- because cancer control programs constitute application of knowledge in the form of demonstrations that such applications are feasible, productive, and effective.

The objective of cancer control is to translate research advances from the laboratory to the practice of medicine and public health, through education, information and demonstration. It does not include research, nor does it include delivery of care -- as such. It does include education of clinicians, allied health personnel; cancer detection; education of the public; relocated motivational studies; application and extension of improved diagnostic methods; rehabilitation of cancer patients, and others. An element of patient care is implicit, particularly in demonstrating, testing the efficacy of new diagnostic and therapeutic regimens, and in the training of clinical personnel. However, the general concept of "delivery of health care," with its attendant broad connotation analagous to the practice of medicine, should not be confused with requirements of cancer control.

Once feasibility of the above elements is initially demonstrated, a function of cancer control is to repeat that initial demonstration as often, and as widely as is necessary to assure that all people have equal access to the very latest diagnostic and treatment capabilities.

At the present time, there are wide discrepancies in sophistication of cancer treatment throughout the country. It is generally true that the cancer patient who lives in an area near a medical educational and research institution if far more fortunate, should he get cancer, than a person living in a predominately rural, low population density area where good medical care may not be available. The situation is improving, but with an aggressive cancer control program, it could improve much more rapidly. This is because in general, research and clinical advances are made in research and educational institutions. Practitioners in proximity to these institutions are stimulated by the pace of progress in research, and their association with the schools and laboratories. Many practitioners in these areas actually serve as part-time faculty members, participating in the educational process as well as benefitting from it. Practitioners are very busy people. The busiest, perhaps, are those in general, or limited specialty practice in the rural, or deprived areas. They have little time to become involved in a wide range of postgraduate, and other professional education activities.

A comprehensive cancer control program will do more than any other effort toward helping people "catch up" with what is known and possible in dealing with cancer. In fact, such a program will be the major part of the national cancer program that will be directly visible to all of the public, and will be the only one they will be able to directly identify with, because through cancer control the National Cancer Program will touch every individual. It is a program for the patient who gets cancer today or tomorrow. In this regard, it becomes a matter of critical importance to the Congress and to the President.

According to National Cancer Institute figures, the most serious casualty of failure to appropriate the authorized $530 million for the Fiscal Year 1973 would be the cancer control program. In the $430 million budget, only $4 million is programmed for cancer control. This amount would be totally inadequate to the needs and opportunities. It would represent only a token effort toward cancer control program development. Of the additional $100 million necessary to bring the appropriation to $530 million, $26 million would be for cancer control. The next two highest increase areas would be research in Cancer Therapy ($18.4 million), and Construction ($17 million). Additon of $26 million would realize appropriation of the full authorization of $30 million in the Act for Cancer Control in 1973.

Effective cancer control requires mobilization of available resources toward it objectives. Money alone will not do the job. The people have to be directly involved. People must be motivated to partake of control programs. The general public must be involved in public education; professionals, such as physicians, dentists, nurses, public health personnel, others, must be involved in professional education.

Recognizing the responsibility of involvement of the private sector in realizing an effective cancer control effort, the American Cancer Society proposes a new concept in the matching of governmental and private effort to reach the objectives of cancer control. The two and one-quarter million volunteers of the American Cancer Society represents an invaluable resource of active, involved citizens, dedicated to the conquest of cancer. These volunteers include 50,000 doctors, who share this commitment, and are actively involved as professionals in pushing back the barriers of inadequate knowledge. Our professional education programs, public information and education programs, cooperation with news media; our program of service to patients, i.e. Reach to Recovery, ostomy programs, programs for teaching laryngectomees to speak -- all represent American Cancer Society resources, public involvement and capabilities that could represent the American Cancer Society share of the proposed "matching" program for effective cancer control.

The National Cancer Institute share of the matching effort could be represented by funds, provision of equipment, supplies, program coordination, etc.. In other words, Mr. Chairman, we are not proposing the traditional "matching" of public and private funds as such, but of public and private resources, organized toward achieving a vital goal, cancer control.

At this point, let me make it clear that the American Cancer Society is not asking that money be granted to it for these programs. Rather, it is expected that National Cancer Institute grants would be made directly to hospitals, institutions, medical schools, or other agencies that would be involved in the programming of activities.

Again emphasizing the need for the earliest possible demonstration of action by the new national cancer program, it is our belief that some control program elements could be instituted very soon and provide that demonstration in an impressive way. In addition, jointly, the American Cancer Society and the National Cancer Institute would demonstrate, in a very productive and meaningful

BEST COPY AVAILABLE

way, the concept of governmental, private sector -- partnership against cancer.

The following are some possible areas of joint, or "matching" effort in Cancer Control:

POSSIBLE AREAS OF JOINT EFFORT IN CANCER CONTROL ACS/NCI

1. Breast Cancer Detection Demonstration Projects
    - a. Purchase of major equipment needed for mammography, xeroradiography and thermography.
    - b. Training programs for:
        1. Diagnostic Radiologists - (to become expert in the techniques)
        2. Radiologic Technicians - (to assist in procedures and to screen results of tests).
    - c. Centralized collection of data and statistical evaluation.
    - d. Construction costs for new facilities and modernization of existing ones.
    - e. Evaluation of ultrasonics and crystallography techniques in diagnosis.
    - f. Hormonal evaluation of high risk groups.
2. Uterine Cancer Control
    - a. Renewal of discontinued Pap smear programs - especially for high density areas where socioeconomic status is low and risk of cerix cancer is high - could be done in conjunction with ongoing family planning services of federal government.
    - b. Clinical investigation of value of irrigation technique for diagnosis of uterine cancer - also the Gravelee aspiration test for endometrial cancer.
    - c. Training Programs for Cytotechnicians

BEST COPY AVAILABLE

d. Investigation of automated techniques for screening

3. Senior Clinical Traineeships in Cancer for internists, surgeons, radiation therapists, diagnostic radiologists and others still in training to provide a core of experts to render clinical care to patients who develop cancer in the next few years.

4. Cancer Education in Medical Schools, Osteopathic Schools and Dental Schools - funds to develop an oncologically oriented curriculum which stresses the interdisciplinary management of cancer. Interest in cancer must be developed at postgraduate level to be properly maintained when patient care responsibility begins. Pilot projects in teaching clinical oncology, programmed instruction courses, etc..

5. Development of Information and Counselling Service for Patients and their Families when cancer strikes.

   Need - trained and informed social workers to advise and direct patients and families to appropriate sources for diagnosis, treatment and post-treatment care. Insurance, employment, management of social problems, etc..

6. Rehabilitation of the Cancer Patient

   Since the effects of cancer treatment often result in some form of disability (e.g. colostomy, laryngectomy, mastectomy, extremity amputation) there is need for more trained physiatrists who can not only render specialized care but also develop training programs of their own to expand the roster of rehabilitation professionals - including allied health professionals (e.g. physical therapists).

7. Colon and Rectal Cancer

   a. Immediate large scale investigation of value of detecting occult blood in the stool in cases of colon and rectal cancer. An inexpensive office and home procedure which needs evaluation very soon.

b. Proctosigmoidoscopy programs in community hospitals and teaching hospitals affiliated with medical schools.

8. Travelling Fellowships for medical students, interns and residents to attend major scientific meetings dealing with cancer. Purpose - to communicate latest research results and to update trainees about modern modalities of therapy.

9. Support of Teams of Travelling Consultants from Cancer Centers - surgeons, radiologists, internists and chemotherapists travelling as small units periodically visit community hospitals and educate local practitioners and advise them on proper use of diagnostic or therapeutic procedures. An important cancer control measure because most cancer patients are diagnosed and treated in community hospitals.

10. Refresher Courses for Practicing Physicians at Existing Cancer Centers - to keep the practicing physician alert to the possible diagnosis of cancer and knowledgeable about management.

11. Special Support of Training Programs in Radiation Therapy to increase the roster of certified radiation therapists in the United States. Currently there is a woefully inadequate supply - about 350 in the entire country.

12. Support of clinical chemotherapy programs in cancer. Provision of high cost medication and germ-free environments to implement and further investigate the burgeoning knowledge about cancer chemotherapy and its promise.

13. Investigation of anti-smoking programs - behavioral science approach to quitting as a preventive measure against lung cancer.

Mr. Chairman, in conclusion, I want to restate, as emphatically as I can, the conviction of the American Cancer Society of (1) the urgent need for funding the $500 million, including $30 million for Cancer Control Programs, authorized for Fiscal Year 1973 by the National Cancer Act; and (2) that the additional $100 million over the recommended budget of the NCI would be wisely, and effectively utilized in the battle against cancer. We urge you, Mr. Chairman, and the Committee to increase this requested budget to $530 million. Thank you.

Travel

S.W.

original given to CGB 3/17/72 by Alan Rabson

AMERICAN CANCER SOCIETY, INC.
219 EAST 42ND STREET • NEW YORK, N.Y. 10017 • (212) 867-3700

LANE W. ADAMS
EXECUTIVE VICE PRESIDENT

March 17, 1972

Mr. Carl G. Baker, M. D.
Director
National Cancer Institute
National Institutes of Health
Bethesda, Maryland 20014

Dear Carl,

Thank you very much for your letter of March 6, requesting opinions from the American Cancer Society regarding our interpretation of Cancer Control as background for your discussions with the National Cancer Advisory Board. As we are well aware of the discussions of cancer control in the Panel of Consultants Report, and of the various objectives and approaches in the National Cancer Plan "Summary of Project Areas", our response will address itself only to immediate needs -- reflecting what we believe to be possible -- and deserving of consideration and action, now, and in the remaining months of Fiscal 1972.

Your request for the views of the American Cancer Society on a number of matters relating to the cancer control element of the National Cancer Program was timely and appropriate, as our Executive Committee met only last week. Therefore, in responding, I am also reflecting the expressed views of our volunteers who serve on that Committee.

We know well and are impressed by the great amount of time and effort by many people -- including representatives of the Society -- that has achieved the present stage of development of a National Cancer Plan. We further recognize the need to devote more time to develop and implement this plan.

cc: Mr. Rassin
Dr. Bruno
Dr. Morrison
Mr. Knight
Dr. [illegible]

In their exhaustive consideration of the legislation, both the President and the Congress emphatically expressed their full commitment and backing of the resulting law. We believe, as I am sure you do, that it is incumbent on all of us to make every effort to meet the challenge they have given us.

The concept of cancer control, to the American Cancer Society, is a critical part of the battle against this disease. Most volunteers serving on our Board, as distinguished from our Research Advisory Committees, have devoted their efforts to so-called cancer control programs. It is therefore understandable that members of the Executive Committee have great interest and concern in the earliest possible implementation of such programs as are realistic and applicable. We believe that this was also the intent of the President and the Congress when they set, and supported the authorization of $420 million for the current fiscal year. Our Committee discussed this last week, and urged that action be taken soon to request a supplemental appropriation of $82 million (including $20 million for cancer control) for the current fiscal year to bring the NCI budget to the full authorization level, thereby enabling programs and projects that should be funded to be started while the longer range planning is underway.

Although cancer control has not been formally defined, to our volunteers it represents the whole range of activities that lies between research and patient care. It does not include research, nor does it include delivery of care -- as such. It does include education of clinicians, allied health personnel; cancer detection; education of the public; related motivational studies; application and extension of improved diagnostic methods; rehabilitation of cancer patients, and others. An element of patient care is implicit, particularly in demonstrating, testing the efficacy of new diagnostic and therapeutic regimens, and in the training of clinical personnel. However, I do not believe that the general concept of "delivery of health care," with its attendant broad connotation analagous to the practice of medicine, should be confused with requirements of cancer control. In fact, I cannot imagine that the Committee intended for all "patient care" to be excluded. However, if this does pose such a problem, I suggest that you ask the principal involved in framing the legislation for clarification.

In justifying a supplemental request for the full amount authorized for FY 1972, we suggest that the objectives of a number of the cancer control programs which were terminated during the past several years be given high priorities quickly and be reinstituted, on a much broader basis than before. Also, we see here an opportunity for the American Cancer Society to support, and participate with the NCI in the planning and conduct of such programs. In fact, recognizing the need for prompt implementation, we believe that our two institutions could demonstrate in a very productive and meaningful way, the concept of governmental private sector -- partnership against cancer -- a "matching program", if you will, of interest, capabilities and effort.

Since both institutions support research programs; jointly sponsor scientific meetings; and maintain close liaison and free exchange of information, we think the ACS could work with the NCI cancer control program in areas such as breast cancer, uterine cancer, colon and rectum cancer, patient information and counselling services, rehabilitation, professional and public information and education programs, and others. A more detailed list of joint program possibilities is attached. Recalling the funding and management problems experienced with the former cancer control programs, under the aegis of the Bureau of State Services, and Regional Medical Program Service, we believe that major improvements can be made in the structure, procedures, and administration of new cancer control efforts.

We are not suggesting the ressurection of old cancer control programs, but rather, an updating, development of matching responsibility areas. This could possibly permit the development of "block" programs, allowing for immediate disbursement of new funds. Any of the attached illustrations would be suitable for funding by grants, and/or contracts. Recipients could be the same kinds of institutions as have received funds for similar purposes in the past.

In presenting our views on the five questions you posed in your letter of March 6th, attached we offer the following responses.

1. The ends oriented objectives of a cancer control program are the elimination of the disease through prevention, diagnosis, and treatment.

BEST COPY AVAILABLE

2. Our views regarding your second question are that a conflict of funding sources and purpose could be resolved "in house", administratively. However, we would hope that the appropriate funds would be used for large scale cancer control programs to confirm research results, for example, the chemotherapy of leukemia, Hodgkins disease, and other cancers, and hopefully, later, immunotherapy. There could be demonstration projects. Also, newer diagnostic tests could be evaluated in large population groups.

3. The immediate success of a cancer control program will be determined by proof of earlier stage of disease at the time of diagnosis. Ultimate success will be demonstrated by a reduction in mortality rates.

4. We recognize your expertise in the intricacies of governmental research administration, and would merely suggest that if this question were posed to the ACS, our response would be based on our conviction of the importance of identifying cancer control as an integral function of the NCI. We would advise obtaining the best qualified, most committed, imaginative person possible, and suggest he report directly to you.

5. Institutions suitable for financing might include medical schools, hospitals, state or county health units whatever agencies most capable for the conduct of the approved programs. Projects and programs might be funded by mechanisms you think most appropriate.

Certainly the overall objective is to reduce the mortality rate in many, if not all forms of cancer. A dynamic cancer control program of the National Cancer Program will achieve this end.

Your letter and this response are being shared with those of our volunteers who serve in committees concerned with legislation and governmental matters.

In our desire to respond quickly with a summary of our views we have not included greater detail about concepts, approaches and methods, but trust that this letter will be adequate for your immediate needs.

Sincerely,

Lane W. Adams

cc: Executive Committee
Legislative Committee
Committee on Federal Programs

Editorial

Restoring Confidence in Mammography

An eloquent passage from the Hippocratic Oath states a basic precept of medicine: "The regimen I adopt shall be for the benefit of my patients according to my ability and judgment, and not for their hurt . . ." In practice, the art of medicine often lies not only in deciding what is beneficial for the patient and what is harmful, but in evaluating which regimen carries the greatest benefit and the least risk. This is the central issue in the current controversy concerning the advisability of mammography. Unfortunately, recent publicity about mammography guidelines has served more to confuse than to clarify.

The guidelines, which are advisory and not regulatory, are derived from the recommendations of committees appointed by the National Cancer Institute and charged with the responsibility of evaluating the possible benefit of screening to find early breast cancer versus the possible risk of inducing breast cancer by radiation exposure. Three groups of women, all of whom had been previously exposed to high or very high levels of radiation, are the basis for the initial statistical evaluation and subsequent predictions of risk.* These women included survivors of Hiroshima and Nagasaki atomic bombings, young women irradiated many years ago for postpartum mastitis, and another group of young tuberculosis patients who had undergone repeated fluoroscopies. The results of this retrospective statistical study suggest that while there may be a theoretical risk from low-dose radiation exposure (after a latency period of many years), the risk is extremely small for the individual woman. Extrapolating from very large doses to very small doses and indicating that there is no absolutely "safe" dose, it is speculated that if a woman has a mammogram, with approximately one rad absorbed by the breast, her chances of developing breast cancer theoretically change from an expected .07 (7.0 percent) to .0707 (7.07 percent). Stated more simply, (if these estimates are applicable) her probability of eventually developing breast cancer is said to increase from one in 14.3 women to one in 14.1 women. Any risk, no matter how small, should not be completely dismissed. At the same time, we must not minimize the risk of spontaneous breast cancer, which remains the leading cancer killer of American women and the leading cause of death in women 39-44 years of age.

The only recognized approach to saving more lives from breast cancer is detection at a localized, highly curable stage, hopefully before the cancer becomes a mass large enough to palpate. Mammography is the only means available today to detect cancer at such an early stage. In the Breast Cancer Detection Demonstration Projects of the American Cancer Society and the National Cancer Institute, at least 45 percent of breast cancers have been detected by mammography alone; the tumors were not found by physical examination. For these minimal tumors, discoverable only by mammography, five-year survival rates of up to 95 percent have been reported, compared to only about 45-50 percent when breast cancer has spread to the axillary lymph nodes.

---

*Report of the Advisory Committee on the Biological Effects of Ionizing Radiations. National Academy of Sciences—National Research Council, Division of Medical Sciences, November, 1972.

The guidelines advise annual screening for *all* women over 50 years old since, in this group, there is no question that the benefits clearly outweigh any minimal long-term risk from radiation. The concept that screening, which includes mammography, has little benefit in women under the age of 50 is based on a 10-year-old Health Insurance Plan study that found no reduction in case fatality rates for screened women in this age group. However, it is noteworthy that the HIP study also showed very few cancers in women under 50 that were detected by mammography alone.

The situation is quite different in the 27 ACS/NCI Breast Cancer Detection Demonstration Projects, largely because mammography techniques have improved vastly over the days since the HIP study was done. At least 233 breast cancers have already been discovered in women under 50 years of age; 100 were detected by mammography *alone*. If mammography had not been used, these early breast cancers would not have been detected at this time. Of the breast cancers found in the Demonstration projects, the incidence of uninvolved axillary lymph nodes is 79 percent for women under and over the age of 50, indicating that these patients have extremely early cancers and represent a highly curable group compared to the usual hospital population with breast cancer.

Who then should have mammography? Certainly, *all women over the age of 50.*

For women between the ages of 35 and 50, mammography should be done for those who are at higher risk of developing breast cancer because they have:

- chronic cystic mastitis, with or without pain;
- lumps and thickenings in the breast;
- nipple discharge or other nipple abnormalities;
- a personal history of breast cancer;
- a family history of breast cancer on the maternal or paternal side;
- a family history of breast cancer in sisters;

- early onset of menstruation;
- no history of pregnancy;
- first full-term pregnancy at age 30 or older;
- breast surgery scheduled for diagnostic purposes;
- fear of breast cancer that requires the reassurance of a negative examination.

Clinicians report that approximately 80 percent of women between 35 and 50 years of age will belong to one or another of the above groups that can benefit from mammography.

The remaining women who are 35-50 years old and those under the age of 35 who have no particular breast problem should be taught the proper technique of breast self-examination and urged to perform it regularly every month. In addition, periodic clinical examinations are warranted. However, many diagnostic radiologists and breast cancer specialists believe that even totally asymptomatic women 35-50 years of age and those under 35 years with a specific breast problem should have at least a baseline mammogram that can be used for later comparisons.

Sadly, many American women have been frightened into believing that mammography represents only a danger, rather than a benefit. This has led a considerable number of women, both over and under the age of 50, to refuse mammography in the presence of symptoms and obvious physical findings and even prior to breast surgery. Any lost opportunity for the earlier diagnosis of breast cancer with its more favorable prognosis must be the current great concern of all physicians.

Of course, the minimum dose required for good mammography should always be used. New equipment is already reducing radiation exposure to extremely low levels that are only a small fraction of the dosage needed 10 years ago.

Breast cancer is so serious a problem, and mammography so valuable a clinical diagnostic aid, that judgments based on fragmentary, tentative or inconclusive data should be avoided. Dr. Francis D. Moore, Moseley Professor of Surgery at Harvard, discussing mass screening for breast cancer by mammography in the September, 1976 issue of *Annals of Surgery*, stated: ". . . one woman in the prime of life found to have an unsuspected cancer that's removed when it's very favorable surgically is a triumph." I concur.

Arthur I. Holleb M.D.

March 1977

WHAT EVERY WOMAN SHOULD KNOW ABOUT BREAST X-RAY

As a means of detecting early breast cancer, a mammogram (breast X-ray) is unequaled. But recent reports suggest that mammography radiation *itself* may increase the cancer risk. To help clear up the confusion, The Reader's Digest offers this interview with a recognized expert

An interview with
DR. BENJAMIN F. BYRD, JR.
1976 President, American Cancer Society

BY WALTER S. ROSS

One out of 13 American women will get breast cancer at some point in her life, accounting for approximately 90,000 new U.S. cases annually. The key to curing a patient with breast cancer is finding it early—before it has had time to invade adjacent tissue. If the disease is treated promptly and properly at this stage, the cure rate can approach 95 percent.

Yet some 33,000 U.S. women will die of breast cancer this year, making it the leading cause of cancer death among women.

THOSE ARE the basic facts about this disease. How are we doing in the battle to lower the high death rate?

The first major step came in the 1950s and early '60s, when a technique for taking X-rays of the soft tissue of the breast was perfected. Then, in 1963, the Health Insurance Plan (HIP) of Greater New York started a randomized study of 62,000 women to see if screening—including use of this technique (called mammography)—could detect more tumors than no screening. In the group that was screened, significantly fewer women over 50 died of breast cancers than in the group that was not. And among women with breast cancers found by mammography alone, only one has died of her disease in the years of follow-up.

Continuing experience proved to doctors that in many women mammography could detect tumors too tiny to be found by any other means. So, starting in 1973, the American Cancer Society and the National Cancer Institute jointly set up a network of 27 Breast Cancer Detection Demonstration Projects. Their purpose: to find out if thorough screening of large groups of women without symptoms, using mammograms and other techniques, could locate more early tumors.

Each project registered 10,000 supposedly asymptomatic women age 35 and over for free examinations to be repeated annually for five years, with a subsequent five-year follow-up. Analysis of the first year's exams of 262,276 women showed that 10,656 biopsies had been recommended, half of these had been performed, and 1248 breast cancers had already been diagnosed. To physicians, these figures meant that active screening was picking up a backlog of hundreds of cancers that probably would not have been detected in the normal course of events for another year or two or three. And this was proved by the fact that subsequent annual rescreenings of the same women found only the expected number of cancers.

Publicity about the projects, and the intense concern women in general have about breast cancer—plus the enormous media coverage of the breast-cancer treatments of Margaretta "Happy" Rockefeller* and Betty Ford—suddenly created an overwhelming demand for mammography. The projects were flooded with applicants.

Then, in mid-1976, a spate of news stories told the public that a single mammography examination could increase a woman's risk of breast cancer by one percent! The scientists who had made the risk-benefit estimate also reasoned that there was no proof that the exams could detect an appreciably greater number of breast cancers in women under 50. They therefore recommended that women under 50 without symptoms should not be exposed to routine mammograms. This information was published in a number of newspapers and broadcast over radio and TV.

The result was nationwide panic. Hospitals from coast to coast reported overnight drops in mammographies of as much as 70 percent. Women with palpable breast lumps canceled their exams. A Detroit radiologist, Dr. John N. Wolfe, wrote to Dr. Theodore Cooper, Assistant Secretary of Health: "I sincerely believe a number of women are going to lose their lives to breast cancer because of the rather extensive publicity."

---

*See "If It Should Happen to You," The Reader's Digest, May '76.

Recent monitoring shows that the breast absorbs less than one rad of radiation in the average mammography examination performed at the NCI-ACS centers. There are no conclusive data on the effects of such low doses of radiation. The scientists who had warned of a possible one-percent increased risk of cancer from mammography had projected downward in a straight line from the proven hazards of high doses toward zero. But no one knows that X-ray risk follows a straight line. Many radiation biologists believe that it does not. In any case, no one knows what happens at very low levels of exposure.

The estimated lack of benefit of mammography in women under 50 was deduced from the 1960s HIP study, which did not show a significantly lower breast-cancer fatality rate among women under 50 who were screened. However, the mammography equipment used then was primitive by today's standards.

Thus the scientists who had sounded the alarm were using a theoretical risk balanced against the results of a study begun a decade earlier. Moreover, the current breast-cancer projects have developed some pertinent new information: about one third—468—of the cancers were found in women between 35 and 50. And of these, 193 were detected with mammography alone.

To help end the current apprehension and confusion about mammography, The Reader's Digest approached Dr. Benjamin F. Byrd, Jr., a distinguished surgeon who served as 1976 president of the American Cancer Society and is head of its Breast Cancer Task Force, for his advice about this important examination.

Q. Dr. Byrd, who should have mammography?

A. In my opinion, women without symptoms who are 35 and over should have at least one mammogram. In young women, the number of tumors found initially will be comparatively low. But mammography is useful even for young women in providing a baseline against which future changes in breast tissue can be judged.

Q. Why wait until 35?

A. This is in asymptomatic women. If a woman has symptoms or is in a high-risk group, her physician may decide that she needs mammography even earlier.

Q. How often should mammograms be done?

A. Mammograms should be done at the physician's discretion in women with a higher than normal risk of breast cancer. In this group, I believe, are women with chronic cystic mastitis; lumps and thickenings in

BEST COPY AVAILABLE

the breast; nipple discharge or other nipple abnormalities; a personal history of breast cancer; a family history of the disease; early onset of menstruation; no history of pregnancy; first full-term pregnancy after age 30. In addition, mammography is a valuable adjunct to diagnosis in women who have unusually large breasts, which are difficult to examine. In the NCI-ACS experience, about 80 percent of women 35 to 50 meet one or another of these criteria.

Q. What, precisely, is the risk in mammography?

A. Nobody knows for sure. Many experts assume that there is risk in any X-ray exposure. If such a risk exists, in this examination it must be very small. More to the point: risk must be placed beside benefit. The results of mammography in discovering early, curable breast tumors are indisputable; such a benefit is real, not theoretical.

Q. Then you're not worried about risk?

A. Every doctor worries about risk, but in mammography the risk is theoretical and can become evident only in 10 to 30 years. If a doctor thinks a woman needs a mammogram, or repeated mammograms, he should do them, I believe—even with younger women. We must remember that breast cancer is the leading cause of death in women between the ages of 40 and 44. If mammography can help save the life of a woman who has many years ahead of her, she is also saved for her family and her children. And even if there is a slightly increased risk of her getting the disease in the distant future, there's also an excellent chance that by that time science will have learned to control breast cancer.

Q. If a woman has a negative mammogram, why does she need another?

A. The incidence of breast cancer goes up with age—age is the biggest risk factor of all. If a malignant change takes place in a breast, it may double in size as often as every 22 days, but more likely every 55 or 110 days, depending on the type of cell. If a cancer is large enough to be seen on mammogram, even though not yet palpable, it is at least 9 months old and probably more than 27 months old. Unless you find and treat it at the earliest stage, you lose the best chance of cure—you want to pick it up as early as possible. And nothing does this better than mammography.

Q. Can you be sure that screening women with mammography is saving lives?

A. The HIP study found that it can in women over 50. It will take more time for our present projects, dealing with women 35 and over, to develop similar proof. But we are seeing some very hopeful things. For example, the first set of examinations in our detection projects, involving some 262,000 women, has yielded more than 1200 cancers. In both younger and older women, we are finding a great number of early cancers. Experience leads us to believe that this will mean many more women will be saved.

BEST COPY AVAILABLE

Q. How about the cost of mammography?

A. For a private examination, this may run from $35 to $100. For the ten-year follow-ups of the 270,000 women in the detection projects, the total cost should be about $75 million—less than the expected cost of a single B-1 bomber. For that money we expect to find 3500 breast cancers among these women in the first five years, and probably more than 2000 in the next five years. We believe that 80 percent will be at potentially the most curable stage, and that several thousand women's lives will be saved. Whether one considers this project cost-effective depends on the value one places on human life. In my view, it is money well and wisely spent.

For information on reprints of this article, see page 230

* * *

Pet Theories

I HAVE A GREAT IDEA for an invention for dieters—a refrigerator that weighs you every time you open the door.

—R. V. Clements, quoted by Earl Wilson, Field Newspaper Syndicate

SOMEWHERE IN AMERICA there has got to be a factory that does nothing but make square wheels for grocery carts. —Don Maclean, United Feature Syndicate

EVERY "ESTIMATE" should be compelled by law to include a footnote estimating how much more than the estimate the final bill will be.

—Sydney J. Harris, Field Newspaper Syndicate

PERHAPS THE CRIME SITUATION would be improved if we could get more cops off television and onto the streets. —Bill Vaughan in Kansas City *Star*

WOULDN'T IT BE SIMPLER just to isolate and label the few things that are *not* injurious to health? —Oren Arnold in *The Kiwanis Magazine*

* * *

Collector's Item: Taxes and tax collectors have always been with us. In my grandfather's papers of more than a hundred years ago, I found an interesting tax bill and statement from the collector in Rouseville, Pa. The back of the bill, dated February 24, 1873, carries this pointed reminder:

Mr. Whittlesee, As you see your taxes amnt. to 3.55. I recd $3.50 which leaves a balance of five cents also five cents for this letter and postage. You need not have an excuse for not knowing what your taxes are for I gave you a notice and afterward told you what it was as we met at Broms shop on the sidewalk.

Ten cents to every man would soon make dollars. W. B. Berman.

—Contributed by Federal L. Whittlesey

Screening for Breast Cancer in Younger Women: Life Expectancy Gains and Losses

An Analysis According to Risk Indicator Groups

Herbert Seidman, M.B.A.

Only three decades ago, uterine cancer was the leading cancer killer of women in the United States. Since then, death rates from cancer of the uterus have plunged downward, the most convincing demonstration of the importance of early detection for the control of cancer.[1] The position of principal cancer killer in women was then assumed by cancer of the breast, a position it has held without challenge to this day.[2] Massive efforts to promote early diagnosis through educational programs on breast self-examination and through emphasis on periodic physical examinations made little dent in the breast cancer death rate, which continued on its inexorable course, unchanging year after year. For too many women, it became evident that even though a lesion in the breast did not appear threatening at diagnosis, the insidious disease had already spread throughout the body. Perhaps without such cancer control efforts the death rate would actually have increased as a result of a presumed increase in breast cancer incidence, but this is small consolation.

The advent of mammography in the 1960s provided a firm basis for the hope that breast cancer in large numbers of women might be detected at an early enough stage to appreciably alter the natural history of the disease. That screening with mammography and clinical examination could lead to a substantial reduction in the breast cancer death rate was then documented in the classic Health Insurance Plan (HIP) clinical trial.[3] I believe that mammography was

Definition of Risk Indicator Groups

Based on Women's Own Statements at Initial Examination*

Major Risk
- Lump in breast
- Discharge from breast
- History of breast surgery
- Family history of breast cancer

Minor Risk (relatively)
- Menarche prior to age 12
- No birth before age 30 of live child

[illegible]

**Excludes women with a history of breast cancer who are known to be at very high risk of a second breast cancer.*

Mr. Seidman is Chief, Statistical Analyses, Department of Epidemiology and Statistics, Department of Research, American Cancer Society, New York, New York.

BEST COPY AVAILABLE

the key to this unprecedented success in breast cancer control. It could hardly have been fortuitous that the death rate was decreased in women over 50 years old, for whom mammography of the 1960s was most effective, and not decreased in women under 50, for whom mammography was much less effective in detecting breast cancer.

It is against this background of decades of helplessness in reducing the tragic toll of breast cancer and the new vistas of hope offered by mammography, that the National Cancer Institute and the American Cancer Society joined forces to sponsor the 27 Breast Cancer Detection Demonstration Projects (BCDDP).[4] The program was designed to screen 280,000 women, ages 35-74 years, annually for five times, using mammography, physical examination, patient history and thermography (the latter was not to be used as a basis for further action, except for scheduling early recall visits). Its purpose was to show that the general public and the medical profession would cooperate to realize the life-saving potential of these procedures in large groups of women.

When these programs were first being planned, there was concern about the possible hazard of radiation exposure from mammography.[5] It was judged that the potential benefits far outweighed the risks[6] and the programs proceeded as planned, starting in 1973. More recently, the question of risk versus benefit has been raised anew.[7,8] While it is generally agreed that there is surely net benefit for women over the age of 50, the situation for younger women is less clearcut.

Younger women comprise a fair-sized proportion of the breast cancer problem, and lives saved in this group would yield more years of life saved than for corresponding numbers of older breast cancer patients. While the rate of clinical surfacing of breast cancer is much lower in younger women, the key question is how many breast cancers might be detected well in advance of the usual surfacing.

On the other hand, the HIP study showed no reduction in breast cancer death rates for younger women. It was thought that benefits would be evident as a result of improvements in mammographic technology, but documentation was not available. In addition, the frequency of breast cancer pickup is likely to be lower in younger women so that the pickup per unit dose of radiation would also be lower. Furthermore, younger women have a longer future lifetime for exposure to the adverse effects of radiation and, from the fragmentary data at hand, they are, if anything, more sensitive to these adverse effects than their older counterparts.[9]

Consequently, pending further study, the BCDDP adopted some interim guidelines for women 35 to 50 years of age. For women at high risk because of family history, reproductive history, prior breast cancer or tumor, etc., the benefits as well as the possible risks of X-ray mammography were to be fully explained to the woman concerned and the final decision made between her and the physician. The routine use of mammography was not recommended for screening asymptomatic women but was not to be withheld if she and the physician agreed that it was in her best immediate interest.[10]

There has been a dearth of solid basic data about breast cancer risk indicators. One aim of this paper is to present new information that will substantially expand our knowledge of the frequency of breast cancer in the various risk indicator groups. However, the principal purpose is to use these and related data to study the risk:benefit ratio of screening in younger women. To do this, I have first constructed a picture of what the breast cancer incidence and life expectancy for the BCDDP women would have been under the conditions prevail-

Table 1
Estimated Breast Cancer Incidence Rates For Risk Indicator Groups By Age*

Summary Risk Indicator Group	Age at Entry (And Number of Women in Cohort)					
	35-39 (38,452 Women)			40-44 (73,976 Women)		
	Percent of Total Women in Cohort	Incidence Rate/ 1,000 Women-Years	Ratio to Rate of "None" Category	Percent of Total Women in Cohort	Incidence Rate/ 1,000 Women-Years	Ratio to Rate of "None" Category
Total women	100.0	0.53	1.15	100.0	1.03	1.18
None	58.2	0.46	1.00	56.8	0.87	1.00
Lump or thickening of breast	3.8	0.82	1.77	3.8	2.14	2.46
Only	2.1	0.81	1.75	1.9	1.81	2.08
Plus other indicators	1.7	0.84	1.82	1.9	2.49	2.86
Discharge from breast	0.8	1.29	2.79	0.6	2.28	2.62
Only	0.3	0.73	1.57	0.2	1.32	1.52
Plus other indicators	0.5	1.74	3.76	0.4	3.02	3.46
History of breast operation	1.6	0.63	1.36	2.0	2.00	2.30
Only	0.7	1.04	2.25	0.9	2.42	2.78
Plus other indicators	0.9	0.29	0.62	1.1	1.65	1.89
History of breast cancer in mother or sister	2.6	1.23	2.65	3.1	2.90	3.32
Only	1.4	0.51	1.09	1.7	1.82	2.08
Plus other indicators	1.2	2.14	4.62	1.4	4.26	3.89
No live child prior to age 30	24.1	0.54	1.17	26.1	1.15	1.32
Only	18.5	0.47	1.02	19.9	0.92	1.06
Plus other indicators	5.6	0.78	1.68	6.2	1.91	2.19
Less than age 12 at menarche	16.7	0.69	1.49	16.2	1.23	1.42
Only	11.7	0.67	1.46	10.9	0.98	1.13
Plus other Indicators	5.0	0.72	1.55	5.3	1.78	2.04

ing in the 1960s (pre-general use of mammography). Comparison is then made with the life expectancy likely to occur among the BCDDP women actually found to have breast cancer at the initial and second annual screenings (1973–March, 1976). Further comparison is made with the life expectancy lost as a consequence of a presumed radiation hazard per unit of radiation.

Material and Methods

The breast cancer picture of the 1960s was developed by using unique data on approximately 560,000 women over 30 years of age. These women were enrolled in a prospective study from October, 1959 through February, 1960 by 68,000 volunteers of the American Cancer Society under the leadership of Dr. E. Cuyler Hammond.[11] Thanks to Dr. Hammond's vision and genius, among the items asked of women at enrollment were questions on current presence of lump or thickening of the breast, current discharge from the breast, his-

[illegible]

Age at Entry (And Number of Women in Cohort)								
45-49 (116,470 Women)			50-54 (105,144 Women)			55-59 (81,131 Women)		
Percent of Total Women in Cohort	Incidence Rate/ 1,000 Women-Years	Ratio to Rate of "None" Category	Percent of Total Women in Cohort	Incidence Rate/ 1,000 Women-Years	Ratio to Rate of "None" Category	Percent of Total Women in Cohort	Incidence Rate/ 1,000 Women-Years	Ratio to Rate of "None" Category
100.0	1.56	1.23	100.0	1.68	1.23	100.0	1.88	1.22
51.4	1.27	1.00	49.0	1.37	1.00	52.5	1.54	1.00
3.7	3.54	2.78	2.5	4.93	3.60	1.7	7.45	4.85
1.6	2.98	2.34	1.0	4.59	3.34	0.7	7.14	4.64
2.1	4.01	3.15	1.5	5.21	3.79	1.0	7.66	4.98
0.4	2.84	2.24	0.3	3.88	2.82	0.2	6.58	4.28
0.1	1.28	1.00	0.1	1.63	1.19	0.1	4.88	3.17
0.3	3.74	2.94	0.2	5.07	3.70	0.1	7.55	4.91
2.4	3.44	2.70	2.4	3.88	2.83	2.1	4.53	2.94
1.0	3.14	2.47	1.0	2.60	1.90	0.9	2.07	1.34
1.4	3.64	2.86	1.4	4.75	3.46	1.2	6.27	4.08
3.9	3.35	2.63	4.3	3.20	2.33	4.8	3.28	2.13
2.0	2.67	2.10	2.1	2.52	1.84	2.5	2.82	1.83
1.9	4.12	3.24	2.2	3.87	2.42	2.3	3.74	2.33
34.2	1.84	1.44	38.7	1.92	1.40	35.5	2.18	1.42
26.8	1.60	1.26	31.2	1.77	1.29	29.0	1.97	1.28
7.4	2.62	2.06	7.5	2.49	1.81	6.5	3.09	2.01
13.8	1.78	1.40	12.2	1.71	1.24	11.3	1.77	1.15
8.3	1.42	1.12	7.1	1.40	1.02	6.9	1.46	0.95
5.5	2.45	1.93	5.1	2.16	1.57	4.4	2.23	1.45

*Based on data from the first five years of the ACS prospective study exclusive of women with a history of breast cancer at entry.

tory of breast operations, history of breast cancer in the subject or her mother or sisters, age at menarche and age at birth of first live child, if any. Subsequent follow-up established which of these women died during the ensuing 12 years, as well as the date and causes of death. In addition, the surviving women completed short questionnaires in 1961, 1963, 1965 and 1972 detailing, among other things, if they had had an operation for breast cancer and the date.

Utilizing this information, the frequencies of breast cancer in the various risk indicator groups were first computed directly and then calculated at the level of the 1969-1971 Third National Cancer Survey (TNCS) incidence rates[12] as follows:

- For five-year age-group cohorts (30-34 years, 35-39 years, etc.) in each risk indicator group note was made of the instances of breast cancer specified for the first five years after enrollment, either on the follow-up questionnaires or as underlying, second or third cause of

Table 2. Estimated Breast Cancer Incidence Rates For Combinations of Major and Minor Risk Indicator Groups By Age*

Summary Risk Indicator Group	Age at Entry (And Number of Women in Cohort)					
	35-39 (36,452 Women)			40-44 (73,976 Women)		
	Percent of Total Women in Cohort	Incidence Rate/ 1,000 Women-Years	Ratio to Rate of "None" Category	Percent of Total Women in Cohort	Incidence Rate/ 1,000 Women-Years	Ratio to Rate of "None" Category
Total women	100.0	0.53	1.15	100.0	1.03	1.18
None	58.2	0.46	1.00	56.8	0.87	1.00
Minors only	33.8	0.56	1.20	34.6	0.99	1.14
One minor only	30.1	0.55	1.20	30.7	0.94	1.08
Two minors only	3.7	0.58	1.25	3.9	1.40	1.61
None plus minors only	92.0	0.50	1.09	91.4	0.92	1.06
One major, total	7.3	0.87	1.89	7.8	2.09	2.39
One major only	4.6	0.75	1.63	4.8	1.90	2.17
One major plus minors	2.7	1.08	2.33	3.0	2.40	2.76
Two or more majors, total	0.7	1.41	3.04	0.8	3.84	4.40
Majors, total	8.0	0.92	1.99	8.6	2.25	2.58

death listed on reports from attending physicians verifying information on death certificates.

- Women with a history of breast cancer at enrollment have been excluded from consideration. These women are known to be at very high risk of a second cancer[13] and there is no good way of distinguishing whether a report of breast cancer during the five-year follow-up period was for a new cancer or was further information on an old one.
- The number of women with breast cancer was then related to the number of years lived by the cohort during the five-year period after enrollment. On the average, a given cohort was two and a half years older during the five-year period than at the start. Therefore, the rates for a given cohort were averaged with the preceding one to see how the absolute rates would compare with the incidence rates from the TNCS. The rates per 100,000 women-years turned out to be 61, 109, 144, 151 and 153 for total women 35-39 years, 40-44 years, 45-49 years, 50-54 years and 55-59 years, respectively. Corresponding rates for the TNCS were 53, 103, 156, 168 and 188. The age-specific rates for women in the various ACS study risk indicator groups were then raised or lowered proportionately so that the rates for total women would be equal to the TNCS rates.

The women who agreed to participate in the long-range ACS Prospective

[illegible]

Age at Entry (And Number of Women in Cohort)								
45-49 (116,470 Women)			50-54 (105,144 Women)			55-59 (81,131 Women)		
Percent of Total Women in Cohort	Incidence Rate/ 1,000 Women-Years	Ratio to Rate of "None" Category	Percent of Total Women in Cohort	Incidence Rate/ 1,000 Women-Years	Ratio to Rate of "None" Category	Percent of Total Women in Cohort	Incidence Rate/ 1,000 Women-Years	Ratio to Rate of "None" Category
100.0	1.56	1.23	100.0	1.68	1.23	100.0	1.88	1.22
51.4	1.27	1.00	49.0	1.37	1.00	52.5	1.54	1.00
39.2	1.59	1.25	42.3	1.67	1.22	39.3	1.85	1.20
35.1	1.55	1.22	38.3	1.69	1.23	35.9	1.87	1.22
4.1	1.92	1.51	4.0	1.48	1.08	3.4	1.58	1.03
90.5	1.41	1.11	91.3	1.51	1.10	91.8	1.67	1.08
8.6	2.87	2.26	7.9	3.08	2.24	7.6	3.77	2.45
4.8	2.81	2.21	4.1	3.03	2.21	4.1	3.52	2.29
3.8	2.95	2.32	3.8	3.13	2.28	3.5	4.07	2.65
0.9	5.80	4.56	0.8	7.58	5.52	0.6	8.71	5.66
9.5	3.16	2.48	8.7	3.48	2.54	8.2	4.16	2.70

*Based on data from the first five years of the ACS prospective study exclusive of women with a history of breast cancer at entry.

Study were not necessarily representative of the general population. However, they do provide a reasonably good approximation of the population of stable women who would be able to commit themselves to five annual screenings. As such, they are an appropriate group to relate to BCDDP women. Also, in both the ACS study and the BCDDP programs, the women's own statements were the basis for establishing risk indicator groups.

BCDDP was formulated as a service demonstration project, not as a research undertaking. Despite the self-selected nature of the women who chose to participate and the problems of achieving some semblance of uniformity among 27 disparate and independent programs, it became apparent that there was a potential for much useful information ancillary to the service aspect.

The evolution of this information gathering poses some difficulties in distinguishing risk indicator groups. The earliest patient history form, completed for about six percent of the BCDDP women, was very cumbersome and consistency with later forms cannot be achieved. Its successor, completed for about 29 percent of the BCDDP women, was still unwieldy but did provide full information on risk indicators. The last patient history form, completed for about 65 percent of the BCDDP women, was a streamlined version, so stream-

Table 3.
BCDDP Results of Initial and Second Annual Screenings
For Summary Risk Indicator Groups
By Age at Entry*

Summary Risk Indicator Group And Screening Series	Age at Entry							
	35-39				40-44			
	No. of Women	Percent of Total	No. of Breast Cancers	Rate per 1,000	No. of Women	Percent of Total	No. of Breast Cancers	Rate per 1,000
Total								
Initial screening	40,951	100.0	41	1.00	45,239	100.0	100	2.21
Interval year 1			21	0.51			26	0.57
Second screening	19,839	100.0	10	0.50	22,423	100.0	43	1.92
Interval year 2			5	0.25			4	0.18
None plus minors only								
Initial screening	26,390	64.4	21	0.80	29,735	65.8	53	1.78
Interval year 1			8	0.30			13	0.44
Second screening	11,391	57.4	7	0.61	13,271	59.2	16	1.21
Interval year 2			1	0.09			3	0.23
One major, total								
Initial screening	12,405	30.3	13	1.05	12,999	28.7	33	2.54
Interval year 1			10	0.81			10	0.77
Second screening	6,757	34.1	1	0.15	7,328	32.7	20	2.73
Interval year 2			3	0.44			1	0.14
Two or more majors, total								
Initial screening	2,156	5.3	7	3.25	2,505	5.5	14	5.59
Interval year 1			3	1.39			3	1.20
Second screening	1,692	8.5	2	1.18	1,824	8.1	7	3.84
Interval year 2			1	0.59			0	0

lined that it omitted information on menarche and childbearing and, in the section on family history of breast cancer, did not specify the particular relatives affected but was limited to the total number of relatives involved.

Because of the enormous volume of data accumulated, some shortcuts have been employed in storing the patient history information on tape. The total form was initially key punched for a sample 10 percent of the women and only the "first" page was key punched for all women. The total form is punched subsequently for any woman recommended for biopsy or found to have breast cancer, etc. This undoubtedly leads to some inconsistencies.

There also are time-lags between the recommendations of actions based on findings at screenings, the accomplishment of these actions, the reports of these actions to the 27 program offices, the transmittal of these reports to the central repository (the Data Management Center, supported by the National Cancer Institute) and the storage of these records on tape. As an aftermath of the July 19, 1976 discussions of the pros and cons of mammography screening,[14] I wanted to make a critical examination of what the BCDDP results might indicate with respect to the risks versus the benefits of screening. To do this, a great deal of information as yet unreported to DMC was necessary. Thus, I requested

[illegible]

Age at Entry											
45-49				50-54				55-59			
No. of Women	Percent of Total	No. of Breast Cancers	Rate per 1,000	No. of Women	Percent of Total	No. of Breast Cancers	Rate per 1,000	No. of Women	Percent of Total	No. of Breast Cancers	Rate per 1,000
48,268	100.0	214	4.43	45,687	100.0	231	5.06	33,412	100.0	218	6.52
		44	0.91			34	0.74			25	0.75
24,213	100.0	55	2.27	22,543	100.0	47	2.08	15,970	100.0	51	3.19
		7	0.29			9	0.40			8	0.50
31,383	65.1	106	3.38	30,098	65.8	125	4.15	21,601	64.7	113	5.23
		15	0.48			10	0.33			11	0.51
14,062	58.0	26	1.85	13,664	60.6	25	1.83	9,340	58.6	25	2.68
		4	0.28			4	0.29			4	0.43
14,211	29.4	74	5.21	13,096	28.7	75	5.73	10,232	30.6	83	8.11
		21	1.48			13	0.99			8	0.78
8,163	33.7	20	2.45	7,220	32.0	15	2.08	5,484	34.3	22	4.01
		2	0.25			4	0.56			4	0.73
2,674	5.6	34	12.72	2,493	5.5	31	12.43	1,579	4.7	22	13.93
		8	2.99			11	4.41			6	3.80
1,998	8.3	9	4.50	1,659	7.4	7	4.22	1,146	7.2	4	3.49
		1	0.50			1	0.60			0	0

*Based on screenings through March, 1976 exclusive of women with a history of breast cancer at initial screening.

that details be obtained from the project offices for all breast cancers detected through June, 1976 as a result of screenings through March, 1976. It was important for me to know whether the cancer was in situ or invasive, the number of axillary nodes examined pathologically and the number found to be positive, the size of the principal mass and the type of treatment. The cooperation of the Project Coordinators was superb. Breast cancer was reported for 1,776 women in the initial screening, the interval to second annual screening, the second annual screening and the interval to the third annual screening. Pathologic reports were available for verifying details for 967 patients; in 809 patients we relied fully on reports from the Project Coordinators. A second breast cancer was specified for 50 women. However, in this paper, only the first cancer detected has been considered or, if two were found concurrently, the one with the poorer prognosis. In addition, women with a prior history of breast cancer at initial examination have been omitted.

The term "screening" as used in this article includes the whole series of visits referable to that screening, as well as early recall visits. The large majority of breast cancers found were pathologically confirmed shortly after the first visit of a series. It sometimes took several months for confirmation, especially if recall visits were involved. Interval

Table 4
Estimated Lead Times for Breast Cancers Detected at Initial and Second Annual Screenings For Summary Risk Indicator Groups By Age at Entry

Summary Risk Indicator Group and Screening Series	Age at Entry 35-39: Rate per 1,000	35-39: Years with Respect to Entry which would Yield Sufficient Usual Incidence	35-39: Mean no. of Years of Lead Time	Age at Entry 40-44: Rate per 1,000	40-44: Years with Respect to Entry which would Yield Sufficient Usual Incidence	40-44: Mean no. of Years of Lead Time
Total						
Initial screening	1.00	0 -2.67	1.33*	2.21	0 -2.25	1.12*
Second screening	0.50	2.67-3.33	2.00*	1.92	2.25-3.48	1.86*
None plus minors only						
Initial screening	0.80	0 -2.84	1.42*	1.78	0 -3.46	1.73*
Second screening	0.61	2.84-4.14	2.49*	1.21	3.46-4.98	3.22*
One major, total						
Initial screening	1.05	0 -2.34	1.17	2.54	0 -1.58	0.79
Second screening	0.16	2.34-2.50	1.42	2.73	1.58-2.82	1.20
Two or more majors, total						
Initial screening	3.25	0 -3.06	1.53	5.59	0 -1.70	0.85
Second screening	1.18	3.06-3.58	2.32	3.84	1.70-2.55	1.13

cancers arose either as newly emergent cancers or as false-negative cancers not detected at screening. There was difficulty in applying consistent rules for classifying the latter cancers. A pending review to achieve uniformity will result in the reclassification of some of these as screening-detected cancers.

These data were the best available at the time (July, 1976). New information is continually accumulating that will change some details both quantitatively and qualitatively, but the updatings are unlikely to seriously affect the overall patterns of our findings.

For the breast cancers detected at BCDDP screenings in the various risk indicator groups, we have estimated the "lead time," that is, the time prior to usual clinical pickup gained by screening detection. This was accomplished by starting with the rates for breast cancer found at the screenings. It was then determined, using very simple assumptions, how far into the future one would have to project to yield these rates if the usual cancer surfacing rates were at the level indicated for that group of women by the ACS Prospective Study, allowing for the aging of the women and the rates of finding interval cancers.

Life expectancy calculations were based on the 1969-1971 United States life tables for women.[15] The age-specific probabilities of breast cancer patients surviving for successive five-year

[redacted]

Age at Entry								
45-49			50-54			55-59		
Rate per 1,000	Years with Respect to Entry which would Yield Sufficient Usual Incidence	Mean no. of Years of Lead Time	Rate per 1,000	Years with Respect to Entry which would Yield Sufficient Usual Incidence	Mean no. of Years of Lead Time	Rate per 1,000	Years with Respect to Entry which would Yield Sufficient Usual Incidence	Mean no. of Years of Lead Time
4.43	0 -3.00	1.50*	5.06	0 -2.89	1.45*	6.52	0 -3.18	1.59*
2.27	3.00-4.15	2.58*	2.08	2.89-3.83	2.36*	3.19	3.18-4.43	2.80*
3.38	0 -3.85	1.93*	4.15	0 -3.79	1.90*	5.23	0 -4.41	2.21*
1.85	3.85-5.63	3.74*	1.83	3.79-5.34	3.57*	2.68	4.41-6.28	4.34*
5.21	0 -2.42	1.21	5.73	0 -2.35	1.17	8.11	0 -2.59	1.30
2.45	2.42-3.32	1.87	2.08	2.35-3.09	1.72	4.01	2.59-3.78	2.18
12.72	0 -2.71	1.35	12.43	0 -2.28	1.14	13.93	0 -1.99	1.00
4.50	2.71-3.43	2 07	4.22	2.28-2.85	1.56	3.49	1.99-2.36	1.17

*Estimated from age and risk indicator group specific incidence rates weighted by the distribution of BCDDP women and allowing for the reallocation of women with a family history of breast cancer aside from mother or sister.

Note: Based on screenings through March 1976 exclusive of women with a history of breast cancer at initial screening.

intervals after diagnosis were computed as ratios of general population survival. Survival data for the usual clinical breast cancer patient for the first 20 years after diagnosis were very kindly prepared for us by the End Results Group based on cases diagnosed from 1950 to 1969.[16] At the end of 20 years (the fourth five-year interval), survivors among patients 35-59 years at diagnosis had attained about 91 percent of the general population survival. The future survival of the cancer patients was extrapolated by assuming convergence to general population survival in another 20 years and normal survival thereafter.

In order to estimate the number of years of life expectancy for the BCDDP breast cancer patients, six categories have been defined on the basis of invasiveness, tumor size and extent of lymph node involvement. These six categories are:

I. In situ;
II. Invasive or unknown invasiveness, no* positive axillary nodes and size < one cm. in diameter;
III. Invasive, no* positive axillary nodes, size one or two cm. in diameter; or one + or unknown positive axillary nodes, size < one cm. in diameter;
IV. Invasive, no* positive axillary nodes and size three + or unknown cm. in diameter; or one

Table 6.
Mean Ratios of Age-Specific Survival Probabilities After Diagnosis of Cancer to Corresponding Survival in General Population of U.S. Women†

Category of Breast Cancer	Periods of Years after Diagnosis							
	0-5	5-10	10-15	15-20	20-25	25-30	30-35	35-40
Total invasive, usual case finding	.63	.81	.89	.91	.93	.95	.96	.98
Cat. I. In situ	.96	.97	.98	.98	.99	.99	.99	.100
Cat. II. Invasive or unknown invasiveness, no* positive axillary nodes and size < 1 cm. diameter	.92	.94	.96	.97	.97	.98	.99	.99
Cat. III. Invasive, no* positive axillary nodes and size 1 or 2 cm. diameter; or 1+ or unknown positive axillary nodes and size < 1 cm. diameter	.85	.88	.93	.94	.95	.96	.97	.99
Cat. IV. Invasive, no* positive axillary nodes and size 3+ or unknown cm. diameter; or 1-3 or unknown positive axillary nodes and size 1 or 2 cm. diameter	.73	.83	.89	.91	.93	.95	.96	.98
Cat. V. Invasive or unknown invasiveness, 1-3 or unknown positive axillary nodes and size 3+ or unknown cm. diameter; or 4+ positive axillary nodes and size 1 or 2 cm. diameter	.61	.77	.86	.88	.91	.93	.95	.98
Cat. VI. Invasive, 4+ positive axillary nodes and size 3+ or unknown cm. diameter	.23	.59	.75	.80	.84	.88	.92	.96

†Mean ratios for age-group 35-39 through 55-59 at diagnosis, by category of cancer.

*Includes unknown status of axillary nodes and less than radical mastectomy.

to three or unknown positive axillary nodes and size one or two cm. in diameter;

V. Invasive or unknown invasiveness, one to three or unknown positive axillary nodes and size three + or unknown cm. in diameter; or four + positive axillary nodes and size one or two cm. in diameter;

VI. Invasive, four + positive axillary nodes and size three + or unknown cm. in diameter.

*Includes unknown status of axillary lymph nodes and less than radical mastectomy.

Categories III, IV, V and VI closely follow the groupings of the Surgical Adjuvant Breast Study (SABS)[17] employed by Shwartz as his Prognostic Classes I, II, III and IV.[18] However, while Shwartz uses 93 percent, 81 percent, 67 percent and 25 percent for these classes directly as the ratios to general population survival for the first five years, these figures were adjusted so that their average, weighted by the SABS distribution of cases, equals the age-specific ratios for total invasive cancer in the End Results Group data. For age-groups 35-39 years through 55-59 years, these average out to 85 percent, 73 percent, 61 percent and 23 percent, respectively. The ratios for Categories III-VI for time intervals subsequent to the first five years were then calculated assuming convergence to general population survival proportionate to that for usual clinical breast cancer.

Categories I and II were regarded as cancers that would only rarely have been encountered in the 1960s. The survival ratios for Category II were arbitrarily assumed to be halfway between 100 percent and the ratios for Category III. The ratios for Category I were assumed to be

Table 6.
Years of Life Expectancy for General Population and for Various Categories of Patients Subsequent to Detection of Breast Cancer By Age at Entry and Screening Series

Category of Breast Cancer	Age at Entry and Screening Series									
	35-39		40-44		45-49		50-54		55-59	
	Initial	Second Annual	Initial	Second Annual	Initial	Second Annual	Initial	Second Annual	Initial	Second Annual
General population	39.95	39.04	35.38	34.49	30.94	30.09	26.67	25.85	22.59	21.81
All invasive cancers, usual case finding	19.07	18.80	17.70	17.45	16.43	15.84	13.27	12.87	11.27	10.99
Category I cancers	36.51	35.76	32.76	31.99	28.93	28.03	24.42	23.66	20.62	19.94
Category II cancers	33.32	32.72	30.33	29.87	27.03	26.09	22.33	21.62	18.78	18.20
Category III cancers	27.66	27.32	25.99	25.50	23.56	22.57	18.59	17.97	15.48	15.07
Category IV cancers	22.14	21.82	20.54	20.24	19.04	18.28	15.26	14.79	12.91	12.58
Category V cancers	17.05	16.76	15.59	15.43	14.78	14.24	12.08	11.74	10.40	10.15
Category VI cancers	6.30	6.19	5.75	5.74	5.72	5.60	5.10	5.01	4.67	4.60

halfway between 100 percent and the ratios for Category II. The ratios for Category I are lower than the virtually 100 percent customary for in situ cancer. They were set this way to compensate for the fact that women with breast cancer are at high risk of a second breast cancer, which may be aggressive. Also, with further investigation, some cancers are established to be invasive, though initially found to be non-invasive. Finally, in some instances, there may be uncertainty about the very classification as cancer and about whether the in situ cancer would ever progress to invasion, if untreated.

The loss of life expectancy as a result of the breast cancers presumably induced by the radiation of mammography has been estimated by first accepting for purposes of calculation, the BEIR report estimates of six breast cancers induced per million women per year per rad to the breast after a latent period of 10 years.[19,20] These figures were then applied to the number of women-years the BCDDP women would be expected to live throughout their lifetime in each five-year period following the latent period. This gave the number of induced breast cancers to be anticipated. Next, these numbers were multiplied by the number of years of life lost per breast cancer, computed as the difference between general population life expectancy and that for the usual clinical invasive breast cancer patient, age being taken into account.

Results

Table 1 presents the breast cancer incidence rates for the various risk indicator groups as delineated by the ACS Prospective Study. A small proportion of the population falls into definitely high-risk indicator groups, that is those with well over twice the rates of the "none" group in most ages. These groups include women who at entry into the study had a lump or thickening of the breast, discharge from the breast, a history of breast operation or a history of breast cancer in mother or sister. I have termed these major risk indicators.

More women fall into groups with incidence rates somewhat higher than those of the "none" group, but not twice as high, such as those with menarche at early age or women who prior to age 30 had not given birth to a live child. These are termed minor risk indicator groups. Subgroups of the minor risk indicator groups, for instance women who first gave birth after age 35, have higher rates than those of their total group, but these rates don't approach twice as high as the rates of the "none" group.

Table 2 shows the breast cancer incidence rate patterns for various combinations of major and minor risk indicator groups in the ACS Prospective Study. In the younger age-groups, the women were predominantly premenopausal and in the older, predominantly postmenopausal. It is well known that there are breast cancer differences according to menopausal status.[21] This makes even more noteworthy the remarkable consistency throughout the various age-groups of progressions of breast cancer incidence rates from low to high, comparing "none," to "minors only," to "one major only," to "one major plus minors," to "two or more majors."

In the absence of a major risk indicator, the minor risk indicator group does not show much elevation in breast cancer incidence rates over the "none" group. Adding another "minor only" to a lone "minor only" shows inconsistent differences in incidence rates as compared with the single "minor only." Many of the history forms of the BCDDP women do not contain data concerning the minor risk indicators. Since there is so little difference in the breast cancer incidence rates, the composite group of "none plus minors only" is a feasible group to study.

Table 3 indicates that the rate of breast cancer detected in the initial screening series of BCDDP women ranged from 1.0 per 1,000 women in the 35-39 age-group to 6.5 for those 55-59 years old. This posed no surprising departure from the usual breast cancer clinical surfacing pattern. For each age-group, rates were lowest in the "none plus minors only" risk indicator group and several times higher in the "two or more majors" group. Again we see no surprising departure from clinical surfacing figures. The progression in the rates are actually sharper than those shown in Table 3 because there is a little overstatement of the rates for the "none plus minors only" group, and a little understatement for the "majors" categories. This is due to the fact that all of the required recoding of the short patient history forms to long forms, has not yet been accomplished.

The pool of breast cancers detectable (and confirmable) at initial screening by the technology and medical procedures employed includes the lifetime accumulation of such cancers, minus those that have already surfaced clinically, and minus preclinical cancers that have already been found through some other special examination. The pool of detectable breast cancers at the second annual screening are those missed at initial screening, plus those that became detectable during the year, minus cancers that showed up as interval cancers during the year (and, at least theoretically, minus those that regressed).

A priori, it may be unclear as to how the detection rates for the two screening series will compare. In Table 3 it may be seen that actually the rates for the second annual screening series were generally about 25 or 75 percent those of the initial series. Except for women 35-39 years, rates were lowest in the "none plus minors only" group and several times higher in the "two or more majors" group in the second screening series as well.

There is a discrepancy between the BCDDP and ACS risk-groups in the assignment of those women with a family history of breast cancer aside from mother or sister. Examination of the re-

Table 7
Number of Women Detected with Breast Cancer
At Initial and Second Annual Screening
For Risk Indicator Groups
By Category of Breast Cancer and Age at Entry

Summary Risk Indicator Group and Category	Age at Entry									
	35-39		40-44		45-49		50-54		55-59	
	Initial	Second Annual	Initial	Second Annual	Initial	Second Annual	Initial	Second Annual	Initial	Second Annual
Total										
Total	41	10	100	43	214	55	231	47	218	51
Category I	7	3	41	8	71	15	62	8	45	9
Category II	8	0	2	4	13	3	21	1	18	5
Category III	5	1	20	10	36	13	54	14	57	18
Category IV	14	5	16	10	58	17	60	12	54	12
Category V	6	1	19	9	30	7	26	3	36	5
Category VI	1	0	2	2	6	0	8	9	8	2
None and minor indicators only										
Total	21	7	53	16	106	26	125	25	113	25
Category I	3	2	21	4	25	10	30	6	22	4
Category II	4	0	1	1	9	1	16	0	11	1
Category III	4	0	11	5	20	5	29	8	30	10
Category IV	7	5	8	3	30	8	35	6	26	5
Category V	3	0	10	2	18	2	12	2	19	2
Category VI	0	0	2	1	4	0	3	3	5	2
One major indicator, total										
Total	13	1	33	20	74	20	75	15	83	22
Category I	3	1	14	3	34	2	24	1	18	4
Category II	4	0	1	3	3	0	2	1	7	4
Category III	1	0	5	3	11	6	18	6	22	6
Category IV	4	0	7	6	15	8	20	2	23	5
Category V	1	0	6	5	9	4	9	1	11	3
Category VI	0	0	0	0	2	0	2	4	2	0
Two or more major indicators										
Total	7	2	14	7	34	9	31	7	22	4
Category I	1	0	6	1	12	3	8	1	5	1
Category II	0	0	0	0	1	2	3	0	0	0
Category III	0	1	4	2	5	2	7	0	5	2
Category IV	3	0	1	1	13	1	5	4	5	1
Category V	2	1	3	2	3	1	5	0	6	0
Category VI	1	0	0	1	0	0	3	2	1	0

Note: Based on screenings through March 1976 exclusive of women with a history of breast cancer at initial screening.

sults among the BCDDP women with fully detailed patient histories suggests that these women belong in the major risk indicator groups. This change in assignment implies that the usual breast cancer incidence rates referable to the BCDDP "none plus minors only" group were roughly 20 percent lower than the corresponding rates in Table 2. Also, instead of the 8.5 percent of Table 2, approximately 10 percent of women would fall into the major risk indicator groups.

Table 3 then demonstrates that the BCDDPs were heavily overweighted with women at higher risk of breast cancer, about 30 percent falling into the "one major" group and six percent into the "two or more majors" risk indicator categories. This connotes that for ages 35-59, the breast cancer frequency for BCDDP women is about one-quarter higher than for women in general, even aside from a possible tendency for further high-risk breast cancer self-selection within risk indicator groups.

It is also evident in Table 3 that there was an even greater representation of

Table 8
Estimated Number of Years of Life Expectancy Gained by Detection of Breast Cancer at Initial and Second Annual Screenings For Risk Indicator Groups and Age at Entry

Summary Risk Indicator Group and Screening Series	Age at Entry: 35-39 — Number of Years of Life Expectancy: For Cancers Detected By Screening	35-39: For Usual Cancer Case Finding Plus Lead Time	35-39: Gained	40-44 — Number of Years of Life Expectancy: For Cancers Detected By Screening	40-44: For Usual Cancer Case Finding Plus Lead Time	40-44: Gained
A. Total Years of Life Expectancy						
Total						
Initial screening	1,079	822	257	2,560	1,868	692
Second screening	260	205	55	982	813	169
None plus minors only						
Initial screening	560	422	138	1,336	1,007	329
Second screening	181	144	37	382	318	64
One major, total						
Initial screening	376	259	117	856	604	252
Second screening	36	20	16	460	367	93
Two or more majors, total						
Initial screening	143	141	2	368	257	111
Second screening	44	41	3	140	128	12
B. Mean Years of Life Expectancy per Breast Cancer						
Total						
Initial screening	26.3	20.0	6.3	25.6	18.7	6.9
Second screening	26.0	20.5	5.5	22.8	18.9	3.9
None plus minors only						
Initial screening	26.7	20.1	6.6	25.2	19.0	6.2
Second screening	25.9	20.6	5.3	23.9	19.9	4.0
One major, total						
Initial screening	28.9	19.9	9.0	25.9	18.3	7.6
Second screening	....	....	...	23.0	18.3	4.7
Two or more majors, total						
Initial screening	20.4	20.1	0.3	26.3	18.4	7.9
Second screening	....	.....	...	20.0	18.3	1.7

higher-risk women among those who returned for the second annual screening. In part, this is attributable to the fact that these women were the early entrants into the BCDDP programs where overweighting with higher-risk women was more pronounced (at least one major risk indicator for 43 percent of the 1973 and 1974 entrants, compared with 31 percent of the 1975 and 1976 entrants). Also, the higher-risk women tended to return for the second annual screening more than the lower-risk ones. Thus, among 1973 and 1974 entrants, the return rates were 82 percent, 87 percent and 88 percent for the "none plus minors only," "one major" and "two or more majors" groups.

Using the data of Table 3 in conjunction with those of Table 2, and the revised incidence rates for the "none plus minors only" group, we have estimated the mean lead time for the breast cancers detected by screening to be about 1.4

[illegible]

Age at Entry								
45-49			50-54			55-59		
Number of Years of Life Expectancy			Number of Years of Life Expectancy			Number of Years of Life Expectancy		
For Cancers Detected By Screening	For Usual Cancer Case Finding Plus Lead Time	Gained	For Cancers Detected By Screening	For Usual Cancer Case Finding Plus Lead Time	Gained	For Cancers Detected By Screening	For Usual Cancer Case Finding Plus Lead Time	Gained
A. Total Years of Life Expectancy								
4,836 1,203	3,642 926	1,194 277	4,257 720	3,282 681	975 39	3,257 753	2,731 676	526 77
2,298 594	1,817 447	481 147	2,323 413	1,801 375	522 38	1,681 354	1,454 353	227 1
1,754 395	1,249 330	505 65	1,388 214	1,048 209	341 5	1,264 336	1,013 276	251 60
784 214	576 149	208 65	544 93	433 97	111 -4	312 63	264 47	48 16
B. Mean Years of Life Expectancy per Breast Cancer								
22.6 21.9	17.0 16.9	5.6 5.0	18.4 15.3	14.2 14.5	4.2 0.8	14.9 14.8	12.5 13.3	2.4 1.5
21.7 22.8	17.2 17.1	4.5 5.7	18.6 16.5	14.4 15.0	4.2 1.5	14.9 14.2	12.9 14.2	2.0 0.0
23.7 19.8	16.9 16.5	6.8 3.3	18.5 14.3	14.0 14.0	4.5 0.3	15.2 15.3	12.2 12.6	3.0 2.7
23.1 23.8	16.9 16.6	6.1 7.2	17.5 13.3	14.1 13.9	3.6 -0.6	14.2	12.0	2.2 ....

Note: Based on screenings through March 1976 exclusive of women with a history of breast cancer at initial screening.

years for the initial screening series and over two years for the second annual screenings. Further details may be seen in Table 4.

Table 5 presents the mean ratios of the various age-groups to general population survival probabilities, which enabled us to obtain the survival probabilities for breast cancer patients. Using these probabilities, the years of life expectancy were calculated for the various cancer categories shown in Table 6. These expectancies show a loss ranging from about 21 years for the usual invasive breast cancer patient at age 35-39 years, to roughly half that for a woman age 55-59 years. Category I-IV cancers show less of a loss, while Category V and VI cancers show more. (Table 6.)

Table 7 indicates the categories of breast cancer detected by screening. A large number of cancers were found in favorable life expectancy categories. This is a requisite condition if screening

Table 9.
Estimated Number of Breast Cancers Induced and Number of Years of Life Expectancy Lost[a] By Risk Indicator Groups and Age at Entry

Summary Risk Indicator Group And Screening Series	Age at Entry					
	35-39			40-44		
	Thousands of Women-Years	No. of Breast Cancers Induced	No. of Years of Life Expectancy Lost	Thousands of Women-Years	No. of Breast Cancers Induced	No. of Years of Life Expectancy Lost
Total						
Initial screening	1,232	7.4	60	1,156	7.0	49
Second screening	578	3.5	27	562	3.4	22
None plus minors only						
Initial screening	794	4.8	39	760	4.6	32
Second screening	332	2.0	16	327	2.0	13
One major, total						
Initial screening	373	2.2	18	332	2.0	14
Second screening	197	1.2	9	180	1.1	7
Two or more majors, total						
Initial screening	65	0.4	3	64	0.4	3
Second screening	49	0.3	2	45	0.3	2

is to show any benefit. It is also essential that there not be a compensating concentration of lethal cancers among those not detected by screening. Scrutiny of the interval cancers (details not shown here) reveals that these cancers tend to be in favorable categories, not in unfavorable ones.

As evident in Table 7, the advantageous distribution of the breast cancers by categories was, in general, only slightly less for those found in the second screening as compared with the initial. This implies that "length bias,"[22] the bias of detecting a disproportionate number of the slower-growing cancers that take longer to surface, was not of any great import here.

The life expectancies in Table 6 were next multiplied by the number of breast cancers in the appropriate category in Table 7 to obtain the number of years of life expectancy for the breast cancers detected by screening. (Table 8A.) The number of years of life expectancy for the usual cancer case finding in Table 8A was calculated by adding the mean lead times from Table 4 to the life expectancies for usual cancer case finding commencing at the ages implied by adding the mean lead times to the ages at screening. The gain by screening detection of breast cancers is then the difference between the number of years of life expectancy for screening detection and for the usual case finding, allowing for lead time.

The gain in life expectancy in terms of the mean per breast cancer detected through screening is presented in Table 8B. There is no consistent trend according to risk indicator groups. Women under 50 years of age show greater gains than those in their 50's. At initial screening, the mean gain for those under 50 is about five to seven years, and for those in their 50's, about two to four years. Overall, these gains represent a reduction of roughly one-third in the loss of life expectancy of the usual clinical

[illegible]

Age at Entry								
45-49			50-54			55-59		
Thousands of Women-Years	No. of Breast Cancers Induced	No. of Years of Life Expectancy Lost	Thousands of Women-Years	No. of Breast Cancers Induced	No. of Years of Life Expectancy Lost	Thousands of Women-Years	No. of Breast Cancers Induced	No. of Years of Life Expectancy Lost
1,024 491	6.1 2.9	36 17	780 365	4.7 2.2	22 10	440 197	2.6 1.2	10 4
666 285	4.0 1.7	23 10	514 221	3.1 1.3	15 6	284 115	1.7 0.7	6 2
301 165	1.8 1.0	11 6	223 117	1.3 0.7	6 3	135 68	0.8 0.4	3 1
57 41	0.3 0.2	2 1	43 27	0.3 0.2	1 1	21 14	0.1 0.1	1 1

*Per rad of radiation to the breast assuming six breast cancers per million women-years per rad subsequent to 10 years after screening for initial screening and second annual screening.
Note: Based on screenings through March 1976 exclusive of women with a history of breast cancer at initial screening.

breast cancer patient.

Table 9 shows the number of breast cancers presumably induced and the number of years of life expectancy lost thereby, per rad of radiation to the breast on the basis of the BEIR report figures. The median radiation-induced breast cancer would occur about 26 years after screening for women 35-39 years at screening, and about 19 years after screening for those 55-59 years at screening.

Table 10 brings together the gains in life expectancy through screening detection of breast cancer from Table 8 and the loss per rad of radiation to the breast from Table 9, and shows the results per 1,000 screenees.

The gains through screening detection of breast cancer per woman screened are modest. The highest gain in Table 10 is .08 years per screenee (78 years per 1,000 screenees). On the other hand, at the dosage level to the breast of one or two rads per screening and even doubling the loss to allow for the sampling variation of the BEIR report estimates, the loss per screenee would range from only .006 years at ages 35-39 (six years per 1,000 screenees) to .001 years at ages 55-59 (one year per 1,000 screenees). Except in the 35-39 age-group, the detection benefit is many times the radiation loss, at least for the initial screening. The 45-49 age-group shows gains paralleling and perhaps exceeding those of women in their 50's.

The expectation that the greater frequency of breast cancer in higher-risk women would yield an increased gain through screening is well borne out by the patterns of gain in Table 10.

Discussion

The definitive way to determine the degree of gain through screening detection of breast cancer in women under 50 years of age would be to conduct a clinical trial. This would involve many women for many years, especially to

Table 10.
Gain Through Screening Detection of Breast Cancer Compared With Loss per Rad of Radiation of the Breast* For Initial and Second Annual Screenings By Risk Indicator Groups and Age at Entry

Summary Risk Indicator Group And Screening Series	Age at Entry			
	35-39		40-44	
	Number of Years of Life Expectancy per 1,000 Screenees		Number of Years of Life Expectancy per 1,000 Screenees	
	Gain Through Screening	Loss per Rad of Radiation	Gain Through Screening	Loss per Rad of Radiation
Total				
Initial screening	6.3	1.5	15.3	1.1
Second screening	2.8	1.4	7.5	1.0
None plus minors only				
Initial screening	5.2	1.6	11.1	1.1
Second screening	3.2	1.4	4.8	1.0
One major, total				
Initial screening	9.4	1.5	19.4	1.1
Second screening	2.4	1.4	12.7	1.0
Two or more majors, total				
Initial screening	0.9	1.5	44.3	1.1
Second screening	1.8	1.4	6.6	1.0

evaluate different strategies~~, such~~ as omitting mammography as part of the present procedure,[23] or establishing the optimal periodicity of repeat screening. Difficult as the problems of ascertaining the dynamic biologic significance of minimal breast cancer may be, to directly ascertain any loss due to radiation exposure would be even more difficult, considering the low level of the dosage and the length of time it would take for an effect to be present, let alone detectable.

This means that alternative methods of assessment, however unsatisfying, are necessary. Several investigators have already constructed mathematical models to estimate the gains of screening.[18,24,25] Their evaluations were based on previously available data. Current estimates presented in this article are based on new data, albeit imperfect, which were developed and applied in a direct, straightforward manner with as few and as simple assumptions as possible. I limited myself to these procedures because of the tentative nature of much of the data.

It may be anticipated that as further BCDDP data accumulate and as the mathematicians have an opportunity to work with the new data, firmer estimates will be made of the gains through screening.

Determining the loss through radiation is bound to remain a knotty problem, however. Putting aside all of the difficulties involved for the low radiation dosage level of mammography in approximating the frequency of breast cancers to be induced many years into the future, there remains the fact that this type of cancer has not been identified. What are its clinical characteristics and

[illegible]

Age at Entry					
45-49		50-54		55-59	
Number of Years of Life Expectancy per 1,000 Screenees		Number of Years of Life Expectancy per 1,000 Screenees		Number of Years of Life Expectancy per 1,000 Screenees	
Gain Through Screening	Loss per Rad of Radiation	Gain Through Screening	Loss per Rad of Radiation	Gain Through Screening	Loss per Rad of Radiation
24.7 11.4	0.7 0.7	21.3 1.7	0.5 0.4	15.7 4.8	0.3 0.3
15.3 10.5	0.7 0.7	17.3 2.8	0.5 0.4	10.5 0.1	0.3 0.3
35.5 8.0	0.7 0.7	26.0 0.7	0.5 0.4	24.5 10.9	0.3 0.3
77.8 32.5	0.7 0.7	44.5 –2.4	0.5 0.4	30.4 14.0	0.3 0.3

*On the basis of life expectancy per 1,000 screenees.
Note: Based on screenings through March 1976 exclusive of women with a history of breast cancer at initial screening.

prognosis? No one knows. In this paper, the life expectancy of a patient with the usual clinical invasive cancer was assigned to the radiation-induced breast cancers calculated by assuming the BEIR report estimates. Certainly one would hope that this is unduly conservative, and that 10, 20 or 30 years from now, much improved therapeutic measures would be available to such patients.

Another difficult problem is whether there is any special radiation effect in the various breast cancer risk groups. Though there is concern about possible synergism of radiation exposure with high-risk breast cancer factors, there is virtually no information. However, it is reassuring that what little information exists, the fragmentary indications from the atomic bomb studies concerning the risk factor of advancing age,[9] does not suggest synergism.

Summary

- Using data from the ACS Prospective Study and excluding women with a history of breast cancer who are known to be at very high risk of a second breast cancer, breast cancer incidence rates are estimated for age-groups 35-39 through 55-59 years for various risk categories defined by the women's own statements. The women with none of the risk indicators, the "none" group, comprised about 54 percent of the total women and showed breast cancer rates, which though the lowest of any risk indicator group, were still quite appreciable, being 80 percent of the rates for total women of their age group.
- Women with menarche prior to age 12 or who had not given birth to a live

child before age 30 showed an excess of 15 percent to 50 percent over the breast cancer incidence rates of the "none" group. These risk indicators are termed "minor" (relatively). The "minors only" group comprised about 38 percent of total women and had breast cancer rates much the same as those of the total women of their age.

- Current breast lump or discharge, or a history of breast surgery or of breast cancer in mother or sister are termed "major" risk indicators. One such indicator was noted for about eight percent of total women and generally denoted breast cancer incidence rates somewhat over 100 percent in excess of the rates of the "none" group. Two or more "major" risk indicators, observed in less than one percent of the women, meant an excess of 200 percent to over 400 percent compared with the incidence rates of the "none" group.
- Using these data in conjunction with information from the initial screening series of the BCDDP women ages 35-59, and similarly excluding women with a history of breast cancer at initial screening, it is found that the BCDDP women are overweighted with high-risk women, having a breast cancer risk about one-quarter higher than the general population.
- The rate of breast cancer per 1,000 women detected in the initial screening series ranged from 1.0 for women 35-39 years to 6.5 for those 55-59 years. The detection rates at the second annual screenings were about 25-75 percent of those at initial screenings.
- It is estimated that the mean "lead time" was about 1.4 years for the breast cancers detected at initial screening and over two years for those detected at the second annual screening.
- Using survival probabilities for the general population from U.S. life tables, and data on the survival of various categories of breast cancer patients, estimates are made of the life expectancies following cancer detection for patients in various categories. As compared with normal expectancy, the usual clinical invasive breast cancer patient is subject to a loss of 21 years of life at ages 35-39 years and about half that at ages 55-59 years.
- Combining the estimates of life expectancy with the number of breast cancers detected in the various categories, data are developed showing the gain in life expectancy through screening. This is computed as the difference between years of life expectancy for the cancers detected by screening, and the years of life expectancy for the usual breast cancer case finding plus mean lead time. The mean gain per breast cancer detected at initial screening for those under 50 is about five to seven years, and for those in their 50's, about two to four years. These gains represent a reduction of roughly one-third in the loss of life expectancy of the usual clinical breast cancer patient.
- Using the BEIR report estimates of six radiation-induced breast cancers per million women per year per rad of dosage to the breast after a 10-year latent period, calculations are made concerning the number of breast cancers presumably to be induced, and the loss in life expectancy thereby. The median cancer case would occur about 26 years after screening of the 35-39 year-old women, and 19 years after screening of those 55-59 years.
- The estimated gains in life expectancy per woman screened through screening detection of breast cancers are seen to be modest. For the initial or second annual screening series, the highest gain among the groups stud-

ied is .08 years per screenee (78 years per 1,000 screenees). For a given screening, the upper limit of the presumable loss due to radiation-induced breast cancers is perhaps .006 years per screenee at ages 35-39 (six years per 1,000 screenees) and .001 years per screenee at ages 55-59 (one year per 1,000 screenees).

- Except in 35-39 year-old women, the estimated detection benefit is many times the presumed radiation loss at initial screening. The expectation that the greater frequency of breast cancer in higher-risk women would yield an increased gain through screening is validated by these data.

The "major" risk indicators delineate a small proportion of women who are at substantially higher risk of developing breast cancer and who show more gain from screening than the large majority of women of their age. However, even without such risk factors, women have an appreciable risk of developing breast cancer. This risk is of sufficient magnitude to alert all physicians to the possible presence of breast cancer at the time of clinical examination.

References

1. Hammond, E.C., and Seidman, H.: Progress in control of cancer of the uterus. Arch. Environ. Health 13:105-116, 1966.
2. Silverberg, E., and Holleb, A.I.: Cancer statistics 1972. CA 22:2-20, 1972.
3. Shapiro, S.; Strax, P.; Venet, L., and Venet, W.: Changes in five-year breast cancer mortality in a breast cancer screening program. In: Seventh National Cancer Conference: Proceedings. Philadelphia: J.B. Lippincott Co., 1973. Pp. 633-678.
4. American Cancer Society: Annual Report, 1974. New York: February, 1975.
5. Communication from Saul Harris (Director, Office of Radiation Control, New York City Department of Health) to Frank J. Rauscher (Director, National Cancer Institute), January 10, 1973.
6. Communication from Kenneth B. Olson (National Cancer Institute) to Saul Harris, (New York City Department of Health), February 8, 1973.
7. Bailar, J.C., III.: Mammography: A contrary view. Ann. Intern. Med. 84:77-84, 1976.
8. Breslow, L.: Progress report submitted to Dr. Guy R. Newell (National Cancer Institute), July 15, 1976.
9. Jablon, S., and Kato, H.: Studies of the mortality of A-bomb survivors. 5. Radiation dose and mortality, 1950-1970. Radiat. Res. 50.649-698, 1972.
10. Fink, D.J., and Holleb, A.: Interim guide line for women under 50. (Letter to Project Directors, Breast Cancer Detection Demonstration Program), August 23, 1976.
11. Hammond, E.C.: Cancer etiology: New prospective epidemiological study. CA 9:177-178, 1959.
12. Third National Cancer Survey. Incidence Data. National Cancer Institute. Cutler, S.J., and Young, J.L. (eds.). Department of Health, Education and Welfare (National Institutes of Health) Publication No. 75-787. National Cancer Institute Monograph No. 41, March, 1975.
13. Robbins, G.F.., and Berg, J.W.: Bilateral primary breast cancer; a prospective clinicopathological study. Cancer 17:1501-1527, 1964.
14. Breast Cancer Detection and Mammography. Transcript of Meeting, July 19, 1976. National Cancer Institute, Bethesda, Maryland.
15. United States Life Tables: 1969-1971, Department of Health, Education and Welfare (HRA) Publication No. 75-1150, Vol. 1, No. 1. U.S. Department of Health, Education and Welfare, Washington, D.C., May, 1975.
16. Unpublished data. End Results Section, National Cancer Institute.
17. Fisher, B.; Slack, N.H., and Bross, I.D.: Cancer of the breast: size of neoplasm and prognosis. Cancer 24:1071-1080, 1969.
18. Shwartz, M.: Analysis of the benefits of serial screening to detect early breast cancer. Michigan Cancer Foundation, Detroit, Michigan, March, 1976.
19. Report of the Advisory Committee on the Biological Effects of Ionizing Radiations: The Effects on Populations of Exposures to Low Levels of Ionizing Radiation (BEIR Report). Division of Medical Sciences, National Academy of Sciences—National Research Council, Washington, D.C., November, 1972.
20. Upton, A.C.: Draft Report, National Cancer Institute Ad Hoc Working Group on the Risks Associated with Mammography in Mass Screening for the Detection of Breast Cancer, August, 1976.
21. Stavraky, K., and Emmons, S.: Breast cancer in premenopausal and postmenopausal women. J. Natl. Cancer Inst. 53:647-654, 1974.
22. Feinleib M., and Zelen, M.: Some pitfalls in the evaluation of screening programs. Arch. Environ. Health 19:412-415, 1969.
23. Zelen, M.: Theory of early detection of breast cancer in the general population. In: Henson, J.C. et al. (eds.): Breast Cancer: Trends in Research and Treatment. New York: Raven Press, 1976.
24. Chiacchierini, R.P.; Lunding, F.G., and Scheidt, P.C.: Summary Progress Report of a Risk Benefit Evaluation of Mammography Screening for Breast Cancer by Life Table Modeling. U.S. Department of Health, Education and Drug Administration, Bureau of Radiological Health, Division of Biological Health, 1976.
25. Blumenson, L.E.: When is screening effective in reducing the death rate? Math. Biosci. 30:273-303, 1976.

Mr. ROGERS. We will have witnesses this afternoon. I think it would be well if somebody from the Cancer Institute would be available for questioning, if we have questions that issue or arise from the next witness.

It is 12:30 now. I am glad to see the change that you have brought about in the guidelines. I think we need to go beyond our own centers to see if the guidelines are being carried out nationwide. I think that it is important that you do this. I am also glad to see the research it is receiving, and I hope it will be vigorously pursued for alternative remedies. You seem to be moving there as well. If we could get this cleared up, about the American Cancer Society, and if those guidelines are consistent with the NCI, it would be helpful. I might ask this: The Pathology Committee of the Beahrs group reviewed, I think, 506 cases of minimal cancers, less than 1 centimeter in size. Of these, they concluded that 66 cases that had been interpreted previously as cancerous should be reclassified as benign. Could you give us a quick comment on that?

Dr. COSTLOW. Yes. The Beahrs Pathology Group is at the present time going through those 66 cases. We do not have a complete report on that, a final report as yet. But as of November, the preliminary report that they provided to us, that number is considerably less than 66, because of a variety of things in the way the review was conducted.

Mr. ROGERS. Have we got any final report at all?

Dr. COSTLOW. No, sir. We are expecting that in about 1 month.

Mr. ROGERS. Would you furnish that to the committee?

Dr. COSTLOW. I certainly will.

Mr. ROGERS. Thank you for your presence today. It has been most helpful.

The committee will stand adjourned until 2 p.m. this afternoon. Thank you for your presence.

[Whereupon, at 12:28 p.m., the hearing was recessed, to resume at 2 p.m., this same day.]

AFTER RECESS

[The subcommittee reconvened at 2 p.m., Hon. Paul G. Rogers, chairman, presiding.]

Mr. ROGERS. The subcommittee will come to order, please.

This afternoon the first witness is Dr. John C. Bailar III, editor in chief of the Journal of the National Cancer Institute, National Cancer Institute, Bethesda.

Doctor, we welcome you to the committee. We are pleased to have you here. We understand that you are submitting a statement for the record and we will be glad to make it a part of the record.

You may proceed as you desire.

STATEMENT OF JOHN C. BAILAR III, M.D., PH. D., WASHINGTON, D.C.

Dr. BAILAR. Thank you, Mr. Chairman, for the invitation to come here and discuss some of the lessons that can be learned from recent experiences with breast cancer screening programs.

I would like to emphasize that I do not present the official views of any governmental agency and my remarks are mine alone. You have heard some of the history of the mammography screening programs. I will not repeat that.

You have also heard of some of the problems and uncertainties that centered on the decision to undertake large scale screening several years ago. To repeat those, there is not yet any direct demonstration of benefit for women at ages 50 or younger. That is not to say there is no benefit; we just have no evidence on that.

Some of the other limitations are that the contribution of mammography to the overall impact of screening is still undetermined. There is reason to suspect serious long-term risks associated with exposure to the X-rays used in the mammographic examination and we have no data on the optimum frequency of screening at this time.

Despite these uncertainties, several years ago there was a very strong move to promote mammography as an important tool in maintaining health, and some physicians began to recommend annual mammographic screening beginning at age 35, or even younger.

At about the same time, the National Breast Cancer Detection and Demonstration Program was planned and developed by the American Cancer Society and the National Cancer Institute.

In May 1975, I presented the first serious critique of the risks and benefits of mammographic screening at a national meeting of cancer research investigators.

Within months, the general nature of the criticisms was common knowledge. Today, just 3 years later, mammography is largely discredited as a screening technique for the detection of breast cancer in women under the age of 50, and the manner in which it is used at older ages has changed markedly.

The radiation doses of earlier years have been reduced, and the medical profession generally has adopted a much more critical and cautious attitude. However, there are still serious problems.

The BENT program of the Bureau of Radiologic Health suggests that up to 40 percent of mammographic examinations have technical problems that may compromise image quality and resolution. Even within the BCDDP, 65 percent of the equipment now in use operates at radiation exposure levels several fold higher than can be attained with the best available technology.

Present guidelines were developed at a large public meeting at NIH in September 1977.

I won't repeat those guidelines. They are basically that annual screening of women without symptoms of cancer should be limited to those over 50 years of age with the exception of younger women who either have had a personal history or a first degree family history of breast cancer.

While I was a critic of the program in its earlier form, I do support these present guidelines though not without some reservations. There are several important and fundamental research problems in breast cancer screening that have not yet been resolved, and in time we may find that these guidelines should be significantly restricted, or perhaps extended. My main reservations have to do with five things: First is the continued failure to demonstrate benefits for women under 50.

Second, the continual uses of methods and experiments that require radiation doses above necessary exposure levels.

Third, the possibility of synergistic effects between radiation and other risk factors for breast cancer, so that high-risk women are most susceptible to additional radiation carcinogenesis.

Fourth, the unknown malignant potential of many breast "cancers" that are not in fact the usual sort of cancer that invades, metastasizes and kills, and

Fifth, the extraordinarily damaging effect of false negative screening reports.

These matters go well beyond the widely recognized hazards of indiscriminate radiation.

I might say my interest in this problem was first generated not by an appreciation of the high risks, but because I thought the benefits might be much smaller than many people had come to believe.

The prompt and widespread acceptance of last September's consensus guidelines by all responsible segments of the medical community has resulted in a remarkably rapid turn-about in medical practice.

Clearly the medical profession can change rapidly. In the present case, the shift toward more cautious use of mammography was from pressures that were both external—public concern—and internal—the inherent good will and concern of many radiologists and other physicians. But how was this episode different from others that may have had a similar beginning?

What happened, and why?

Why was mammography promoted so heavily when its limitations were already known or could have been known?

What organizations and what persons were responsible?

Who may have been harmed, and what is being done by way of restitution or to limit the harm?

Perhaps no one person knows the full story, but I have seen some parts of it from the inside.

As Deputy Associate Director and Acting Associate Director of the newly-established cancer control program at NCI in 1972 and 1973, I was a concerned and reluctant participant in some of these early activities.

Attachment 2 shows that doubts about mammography were widespread by early 1973, though they were not well publicized.

It is interesting and significant that these doubts came from persons trained in epidemiology and biostats. All of the other professional groups involved did not see the problem so clearly.

There are several important lessons that I believe can be learned from what could be called the rise and partial fall of indiscriminate mammography.

The first and most important lesson is that there was no one to protect the public interest—no person or agency that could effectively identify and eliminate hazardous, unnecessary exposure to low-level radiation.

The cancer-oriented organizations, both public and private, failed.

The ACR, representing the vast majority of physicians controlling the medical uses of X-rays, placed and still places the interests of its members before those of the public.

The Bureau of Radiologic Health has not even yet asked for public comment on the matter, though they plan to do so.

I understand that there is still some dispute within the Bureau as to whether they will include any interim guidelines.

I should mention that there have been some outstanding or partial exceptions to this. The BENT program has been a very laudable effort to find out what radiation doses have been used.

The Environmental Protection Agency, I feel, did try to take the lead in developing guidelines, although I understand third and fourth-hand that they were subject to some hampering and harassment and were not able to come forward with the guidelines that they originally thought were appropriate.

Finally, the National Cancer Institute, where I work, did change its position on these matters. I think that is the most heartening example of the fact that governmental agencies and governmental programs can be self-corrected.

My own involvement was almost accidental. Radiation hazards were not a part of my official responsibilities, and I became interested and active only by default.

Mr. Chairman, I believe that this committee could perform an important public service by assuring that some appropriate agency of the Federal Government takes and effectively uses the responsibility for guarding the public against the hazards of low-level radiation in medicine.

The second lesson is that independent nonprofit voluntary health organizations, such as the American Cancer Society, have their own interests, goals and biases. If government officials forget this fact, the public may suffer.

I don't see any purpose at this point of citing examples, but I think it may be almost self-evident that no two organizations with different responsibilities and different orientations are likely to agree completely on anything.

A third lesson to be learned from the experience with mammography is that decisions on major medical policy are too important to be left to physicians alone. They are likely to be too close to the matter to be sufficiently objective.

The BCDDP was developed and implemented largely by physicians who sincerely believed, as many continue to believe, that mammography was harmless and highly beneficial, but who also had a strong professional and economic stake in the success of the program. Such persons should have been a distinct minority in a decisionmaking process that included larger numbers of surgeons, pathologists, health physicists and biologists, epidemiologists, public health experts, and—most important—informed and critical members of the population to be screened. A few such persons were included, but not enough.

Another lesson to be learned from the BCDDP is that overdiagnosis of cancer can be a serious matter in cancer screening programs.

This occurred with mammography in the BCDDP, though not with breast cancers found by physical examination or medical history.

According to the so-called Beahrs Committee Report, by mid-1976 the BCDDP had reported a total of 1,810 cancers found in close to one-half million examinations. Of the 1,810 cases reported, 592 were described as minimal cancers.

A group of eminent pathologists examined slides for 506 of these minimal cancers and concluded that 66 were entirely benign.

This fact is particularly significant because the promoters of mammography have placed great emphasis on detection of minimal cancers as proof that screening is beneficial. Despite contrary statements by some members of the Beahrs Committee, the pathology review group stands by its original opinion on each of these 66 benign lesions, except for two cases in which the original classification was ascribed to computer error and 16 in which the classification as "benign" led to the submission of additional slides reported to be from the same patient.

We do not, of course, have definite knowledge about the 86 cancers not even submitted for review; but some skepticism may be in order until we can learn why they were not submitted.

The fifth lesson is the necessity for thorough, informed, disinterested assessment of costs, risks and benefits at the earliest stages of planning for vast new health programs. I am aware that some people believe such analyses are impossible, or at least improper, when human health and survival are at stake.

I simply disagree. Such analyses of breast cancer screening could have been done in 1972, and they would have spared many problems for both screenees and the medical profession.

I believe that the implications of this story are important to this committee as it considers how the Government should support health services of all types.

I am not prepared to offer any recommendation on that topic in general, but, whatever the mechanisms that are eventually developed, I urge very strongly that the biases of all the various interest groups be fully balanced by other, disinterested views.

The recent problems with mammography are just one illustration of the unconscious subversion of the public good to private interests. I am not here talking about the orientation of so much medical training and practice toward the management of disease rather than the preservation of health, or about the pervasive and harmful effects of keeping one eye on malpractice insurers and the other on lawyers rather than keeping both eyes on one's patients. Though there are obvious and well-known defects in both crisis medicine and defensive medicine, I believe that the problems are much more deeply rooted and much more difficult to deal with than either of these.

A final lesson has to do with whistle blowing. One person, or a very small group of people, can make a difference, though it may require a great deal of hard work and dedication, a thick skin, and a willingness to step down from positions of prestige and influence while the issue is under debate.

I hope that other public servants will be encouraged to speak up and speak out when there is good reason to question official policies. I hope also that they will be kept free from harassment by their own agencies, as to some extent I was. Perhaps this committee can help.

In conclusion, Mr. Chairman, the most important battle over breast cancer screening may be won, though some debate is likely to continue for many years. General awareness of the need to balance the benefits of screening with its risks has increased to the point where it will insure continued improvement of the program. These improvements should further define the optimum design and application of breast cancer screening programs to guarantee that they are neither too broad nor too narrow, but rather serve the best interests of the public welfare.

Thank you.

Mr. ROGERS. Thank you very much for a very helpful statement. If you wish to include your formal statement at this time we will include it in the record.

I must say too I want to commend you for being willing to personally testify because I understand the problems a person might have working in the Institute where there could be a problem. But I am sure with the new leadership that will not be so.

Dr. BAILAR. I am sure also, sir, that with the new leadership there would not have been any problem. I thought, though, that to avoid any suggestion that my testimony might have been influenced, it was best to proceed this way.

[Testimony resumes on p. 1102.]

[Dr. Bailar's prepared statement and attachments follow:]

STATEMENT OF

Dr. John C. Bailar III

National Cancer Institute, Bethesda, Maryland

14 July 1978

Mr. Chairman, thank you for the invitation to discuss with this Committee the lessons that may be learned from recent experiences with breast cancer screening programs. As a result of my official duties at the National Cancer Institute, I have been deeply involved in certain aspects of the controversy surrounding the use of X-ray mammography. Although I am here today as an employee of the National Cancer Institute, I do not present the official views of any governmental agency. My remarks are mine alone.

It is not easy to to talk about the lessons to be learned from breast cancer screening programs, but only because there are so many such lessons. I will concentrate on several that seem to have particular relevance to the responsibilities of this Committee. First, though, I would like to summarize developments of the past several years.

Mammography is a type of X-ray examination that may be used to find breast cancer before it has spread to other parts of the body. It is believed that early detection will result in more effective treatment, which in turn will result in a better cure rate for the disease. Mammography has been a recognized medical technique for several decades. In 1961, a large-scale clinical trial was initiated to help determine whether screening (defined as the search for breast cancer in asymptomatic women) could effect significant reductions in breast cancer mortality. This study, conducted by the Health Insurance Plan (HIP) of Greater New York, showed that annual screening by a combination of techniques (medical history, physical examination and mammography) can reduce mortality from breast cancer for women over age 50 by approximately 40 percent. However, that study showed no evidence of benefit for women at ages 50 or younger. Other limitations are that the contribution of mammography to the overall impact of the experimental screening program could not be determined from the HIP data, there are serious long-term risks associated with exposure to the X-rays used in the mammographic examination, and no data on the optimum frequency of screening are available.

Despite these uncertainties, about 1972 there was a very strong move to promote mammography as an important tool in maintaining health, and some physicians began to recommend annual mammographic screening beginning at age 35, or even younger. At about the same time, the national Breast Cancer Detection and Demonstration Program (BCDDP) was planned and developed by the American Cancer Society (ACS) and the National Cancer Institute (NCI). By Fiscal Year 1976 the BCDDP was supporting 27 separate screening centers at an annual cost of nearly eight million dollars, over 80% of which came from the government.

In May 1975, I presented the first serious critique of the risks and benefits of mammographic screening at a national meeting of cancer research investigators. Within months the general nature of the criticisms was common knowledge. Today, just three years later, mammography is largely discredited as a routine screening technique for the detection of breast cancer in women under the age of 50, and the manner in which it is used at older ages has changed markedly. More specifically, the radiation doses of earlier years have been reduced, and the medical profession generally has adopted a much more critical and cautious attitude. However, there are still serious problems. The BENT program of the Bureau of Radiological Health suggests that about 40% of mammographic examinations have such serious technical problems that image quality and resolution may be compromised. Even within the BCDDP, 65% of the equipment now in use operates at radiation exposure levels 8-fold higher than can be attained with the best available technology.

Present guidelines on breast cancer screening were developed at a large public meeting at NIH in September 1977. These "Consensus Guidelines" have been summarized by Dr. Samuel Thier as follows, in a paper in the New England Journal of Medicine (297, 1065):

"It seems reasonable to screen women over 50 years

> of age with a combination of physical examination and X-ray mammography. Mammographic equipment should be well calibrated, and the dose of radiation should be less than 1 rad. The patient should ask for and keep a record of her radiation exposure. Women under 50 may continue to be screened by physical examination, but should be screened with X-ray mammography only if they have already had breast cancer or if they are between the ages of 40 and 49 and have a mother or sister who has had cancer of the breast. Though the risk from X-ray mammography may be small, it is finite, and must be balanced against the absence of any demonstrable benefit from screening women below 50 years of age. When screening is done, it should probably be on a yearly basis. Lesions of less than 1 cm should be evaluated by more than two pathologists before any definitive operation is performed, and before a firm diagnosis of cancer is reported to the patient."

I support those guidelines, though not without some reservations. Several important and fundamental research problems in breast cancer screening have not yet been resolved, and in time we may find that these guidelines should be significantly restricted, or perhaps extended. My main reservations have to do with:

1) The continued failure to demonstrate benefits for women under age 50,

2) The continued use of methods and equipment that require radiation doses above necessary exposure levels,

3) The possibility of synergistic effects between radiation and other risk factors for breast cancer, so that high-risk women are most susceptible to additional radiation carcinogenesis,

4) The unknown malignant potential of many breast "cancers" that are not in fact the usual sort of cancer that invades, metastasizes, and kills, and

5) The extraordinarily damaging effect of false-negative screening reports.

These points are discussed at greater length in Attachment 1 to my remarks. Note that they go well beyond the widely recognized hazards of indiscriminate radiation and that none of these three points are fully resolved by reductions in radiation dose.

The prompt and widespread acceptance of the "Consensus" guidelines by all responsible segments of the medical community has resulted in a remarkably rapid turn-about in medical practice. It is in sharp contrast to the more usual situation in which easy, apparently safe, profitable medical procedures proliferate rapidly but fade from use only slowly, or not at all. Clearly, the medical profession can change rapidly. In the present case, the shift toward more cautious use of mammography was from pressures that were largely external (public concern) but partly internal (the inherent good will and concern of many radiologists and other physicians). But how was this episode different from others that may have had a similar beginning? What happened, and why:

Why was mammography promoted so heavily when its limitations were already known, or could have been known?

What organizations and what persons were responsible?

Who may have been harmed, and what is being done by way of restitution or to limit the harm?

Perhaps no one person knows the full story, but I have seen some parts of it from the inside.

As Deputy Associate Director and Acting Associate Director of the newly established Cancer Control Program at NCI, I was a concerned and reluctant participant in some of these early activities. Attachment 2 shows that doubts about mammography were widespread by early 1973, though they were not well publicized. In August 1973, largely because of concern resulting from inability to influence the rapidly developing plans for the BCDDP, I asked to be relieved of all responsibilities in the Cancer Control Program and to be transferred to other duties where I could more effectively voice my concern.

I do not now have access to all relevant documents from that early period. However, it was clear then, as it is now, that taxpayers' funds were being used largely at the direction of, and to support the objectives of, the ACS and the American College of Radiology (ACR). While a few senior NCI officials were deeply involved in the program, I believe that the troubles which later developed are largely related to the separation of responsibility from authority. This separation was of two types. The first was the nearly complete delegation to the ACS of major control over the design of the program, selection of contractors, and monitoring of progress in the screening activities. The second separation was within the NCI, where the limited programmatic authority that was retained within the Institute was, until July 1976, lodged in the Division of Cancer Biology and Diagnosis, while financial control rested with the Division of Cancer Control and Rehabilitation. The spirit of that time is illustrated in Attachment 3, which states, in part,

> "This project has limited objectives and they have been pretty much dictated by the American Cancer Society. In summary they are: 'Can American Cancer Society volunteers mobilize a large number (100,000 per year) of volunteers for thermography, mammography, and a physical exam'?"

There are several important lessons to be learned from this situation. The first and most important lesson is that there was no one to protect the public interest -- no person or agency that could effectively identify and eliminate hazardous, unnecessary, exposure to low-level radiation. The cancer-oriented organizations, both public and private, failed. The ACR, representing the vast majority of physicians controlling the medical uses of X-rays, was not as active concerning protection of the public from radiation risks as it should have been. The Bureau of Radiological Health has not even yet asked for public comment on the matter, though they plan to do so. My own involvement was almost accidental. Radiation hazards were not a part of my official responsibilities, and I became interested and active only by default. Mr Chairman, I believe that this Committee could perform an important public service by assuring that some appropriate agency of the Federal Government takes and effectively uses the responsibility for guarding the public against the hazards of low-level radiation in medicine.

The second lesson is that independent nonprofit voluntary health organizations have their own interests, goals, and biases. If government officials forget this fact, the public may suffer. I will cite two ways in which the public welfare was subordinated to the private interests of the ACS. First, requests for financial support of local screening programs - to be paid largely from government funds - were initially filtered through the various levels of the ACS. Those government contracts were not advertised, and they were not subject to the usual procedures of competitive bidding. Only those proposals generated and then approved by the ACS were forwarded for consideration by the NCI. Of course, this could be seen as relieving the government of a heavy burden in reviewing proposals that would be ineligible for joint support because of ACS opposition, but it opens the way for serious abuses, such as limiting approvals to hospitals and clinics agreeing not to compete with ACS in various fund-raising activities. I understand that this may have happened, and I regret that I cannot be more specific in raising this as a possibility.

The other example is drawn from my own experience. As I first raised doubts about the BCDDP, and as those doubts later gained some support, persons closely affiliated with the ACS sought to have me officially silenced. It is in the nature of things that those actions were never fully reported to me, and it seems likely that most were never recorded or put in writing. I do, however, know of one letter from a former official of the ACS who sought to have my talk removed from the agenda of the November 1976 White House Conference on Breast Cancer. I am grateful that my talk could be given as scheduled: the published version is included here as Attachment 4.

Outsiders can only guess at reasons why the ACS, guided by a handful of the senior members of its National Office, was so intransigent in its support of mammography. One guess is institutional inertia; large programs once started are hard to change. Another guess is reluctance to admit that there might be any defects in a program that was, until recently, a financial bonanza. While the ACS has provided a small proportion of the money for the BCDDP, it has converted that support into enormous amounts of free, favorable publicity, which for an agency supported by public contributions means income. A third guess at reasons for the stubbornness of the ACS in resisting any change or reduction in mammography screening programs is fear of wide-scale protests or even suit by women who have been screened and who may develop breast cancer in the future - a fear that seems well grounded. There does not seem to have been any serious consideration of whether women already exposed to radiation risks should be notified, though BCDDP screenees are so informed in the consent form now in use. Whatever the reason, both the ACS and the public have been badly served. It is ironic, though, that this very intransigence made the task of the critics easier: The supporters of indiscriminate, broad-scale mammography did not take serious scientific criticism seriously until it was too late to keep the issue from coming to general attention.

A third lesson to be learned from the experience with mammography is that decisions on major medical policy are too important to be left to physicians alone. They are likely to be too close to the matter to be sufficiently objective. The BCDDP was developed and implemented largely by physicians who sincerely believed, and may continue to believe, that mammography was harmless and highly beneficial, but who also had a strong professional and economic stake in the success of the program. Such persons should have been a distinct minority in a decision-making process that included larger numbers of surgeons, pathologists, health physicists and biologists, epidemiologists, public health experts, and - most important - informed and critical members of the population to be screened. A few such persons were included, but not enough.

When guidelines similar to those I have just cited were first sent to the 27 BCDDP screening centers, there was open defiance of NCI authority in this matter. A full 75 percent of women under age 50 were claimed to fall under the exceptions. Only some months later, when the threat of contract termination was clearly transmitted and clearly perceived, was that figure cut to its current level of less than 15 percent.

Another lesson to be learned from the BCDDP is that over-diagnosis of cancer can be a serious matter in cancer screening programs. This occurred with mammography in the BCDDP, though not with breast cancers found by physical examination or medical history. According to the so-called "Beahrs Committee Report", by mid-1976 the BCDDP had reported a total of 1810 "cancers" found in close to one-half million examinations. Of the 1810 cases reported, 592 were described as "minimal cancers." A group of eminent pathologists examined slides for 506 of these minimal cancers and concluded that 66 were entirely benign, 22 were noninvasive but could not be definitely classified as benign, and 262 were considered noninvasive neoplasms. Thus there was no evidence that 350 lesions, or 70 percent of the "minimal cancers" reviewed by this group, presented any real threat to life and health. This fact is particularly significant because the promoters of mammography have placed great emphasis on detection of "minimal" cancers as proof that screening is beneficial. Despite contrary statements by some members of the Beahrs Committee, the pathology review group stands by its original opinion on each of these 66 benign lesions, except for two cases in which the original classification was ascribed to "computer error" and 16 in which the classification as "benign" led to the submission of additional slides reported to be from the same patient. We do not, of course, have definite knowledge about the 36 "cancers" not even submitted for review, but some skepticism may be in order until we can learn why they were not submitted.

This is a serious matter, but more serious is the large group of noninvasive neoplasms (262 of the 506 lesions reviewed). We simply do not know what proportion of these neoplasms will ever progress to the more usual forms of breast cancer that invade, metastasize, and kill. That some will do so is likely, but the proportion must be small. No physician would want to be responsible for ignoring a potentially curable cancer, but certainly it is a mistake in medical judgment to recommend a radical mastectomy on the basis of a single reading of a small lesion of doubtful character.

The fifth lesson is the necessity for thorough, informed, disinterested assessment of costs, risks, and benefits at the earliest stages of planning for vast new health programs. I am aware that some people believe such analyses are impossible, or at least improper, when human health and survival are at stake. I simply disagree. Such analyses of breast cancer screening could easily have been done in 1972, and they would have spared many problems for both screenees and the medical profession. Attachments 2 and 5-8 show that early concerns were common knowledge among epidemiologists and statisticians.

I believe that the implications of this story are important to this Committee as it considers how the government should support health services of all types. I am not prepared to offer any recommendation on that topic in general, but, whatever the mechanisms that are eventually developed, I urge very strongly that the biases of all the various interest groups be fully balanced by other, disinterested views. The recent problems with mammography are just one illustration of the unconscious subversion of the public good to private interests. I am not here talking about the orientation of so much medical training and practice toward the management of disease rather than the preservation of health, or about the pervasive and harmful effects of keeping one eye on malpractice insurers and the other on lawyers rather than keeping both eyes on ones' patients. Though there are obvious and well-known defects in both "crisis medicine" and "defensive medicine," I believe that the problems are much more deeply rooted and much more difficult to deal with than either of these.

A final lesson has to do with whistle-blowing. One person, or a very small group of people, can make a difference, though it may require a great deal of hard work and dedication, a thick skin, and a willingness to step down from positions of prestige and influence while the issue is under debate. In my own case, this change in assignment could even be regarded as helpful; it allowed me sufficient free time to work on the matter, as well as significant detachment and freedom from interference by other members of the NCI staff. Because of recent changes in leadership and direction at the NCI, one could not even say that I have suffered any long-term damage to my professional career or reputation, and my role has been officially recognized by a commendation medal.

I hope that other public servants will be encouraged to speak up and speak out when there is good reason to question official policies. I hope also that they will be kept free from harrassment by their own agencies, as to some extent I was. Perhaps this Committee can help.

In conclusion, Mr. Chairman, the most important battles over breast cancer screening have been won, though some debate is likely to continue for many years. General awareness of the need to balance the benefits of screening with its risks has increased to the point where it will insure continued improvement of the program. These improvements should further define the optimum design and application of breast cancer screening programs to guarantee that they are neither too broad nor too narrow but rather serve the best interests of the public.

ATTACHMENT 1

IAEA-SM-224/714
International Symposium on the Late
Biological Effects of Ionizing Radiation
Vienna, March 15, 1978

John C. Bailar III
National Cancer Institute
Bethesda, Maryland 20014 U.S.A.

ABSTRACT

X-ray mammography delivers significant amounts of ionizing radiation to the breast, and the female breast is more susceptible to radiation carcinogenesis than any other human organ. On the contrary, breast cancer is least likely to cause serious illness and death when it is detected at a very early stage.

The risks and benefits of mammography can be estimated. This paper summarizes current risk estimates, then proceeds to a comparison of risks and benefits. As for breast cancer mortality, addition of mammography to a program of annual breast examinations of average U.S. women is of questionable value for women under age 50 but it is probably beneficial for older women. However, the break-even point is closely related to the average radiation exposure of breast tissue and would be earlier in a few centers now using optimum techniques and equipment. For women with below-average risks of breast cancer, the age would be higher, and for a few women with a high probability of developing breast cancer it would be lower. The break-even point should be significantly exceeded before mammographic screening becomes worth the time, trouble, and other costs.

Breast cancer screening programs have been improved significantly since criticisms were first publicized in mid-1975. Partial improvements include reduction in radiation exposure (at least in some centers), guidelines from the National Cancer Institute (NCI) and the American Cancer Society (ACS) for restricting the screening of women under age 50, and changes in the patient consent form signed by screenees in the NCI-ACS program. Professional and public awareness of the need to balance the benefits of screening with its risks and costs has rapidly and markedly increased. Future improvements should further define the optimum design and application of breast cancer screening programs.

- -

In the United States there has been much public debate (and much public misunderstanding) about the benefits and risks of breast cancer screening. This paper briefly reviews the history of this debate, assesses the data on which decisions must be based, comments on the many serious questions remaining, and describes current guidelines. Radiation hazards have been important elements in the debate, and their impact on opinions and conclusions will be described. Various aspects of this matter have been discussed in other publications (1-3), with which this paper forms a continuous series.

In this paper, "screening" refers to the periodic examination of women who have no symptoms that specifically suggest breast cancer. Thus the diagnostic study of suspected cancers is excluded. Most women have minor breast complaints from time to time; such women are not considered symptomatic unless there is real suspicion that the symptoms may indicate cancer.

This paper does not reexamine the basic data on radiation carcinogenesis in the human breast. Upton et al. (4) recently considered all available human data suitable for this purpose; no additional data have been reported since then; and I know of no other significant data sources that could add to our knowledge on this matter within the next few years. Upton et al. concluded that,

> "... the risk may be assumed to approximate 3.5-7.5 cases of breast cancer per million women of ages 35 or older at risk per year per rad to both breasts, from the tenth year after irradiation throughout the remainder of life."

I accept that estimate as the best that can be derived today. It implies a strictly additive, linear, nonthreshold dose-response relationship, and those who believe that other models should be used may come to significantly different risk estimates. [For discussion of these points see (5-11).] This estimate also implies that the female breast is one of the most sensitive human organs for radiation carcinogenesis (12). This fact is important in determining how X-ray examinations of the breast, called mammography, should be used in screening programs.

The well-known study of the Health Insurance Plan of Greater New York (H.I.P.) (13) showed, beyond serious question, that annual screening by a combination of modalities (medical history, physical examination, and mammography) can reduce mortality from breast cancer for women over age 50. The mortality reduction was almost 40% in that age group, a result of great practical importance. In contrast, no mortality reduction whatever occurred in younger women. These results refer to the effect of the three screening modalities together. The H.I.P. study was not designed to provide reliable assessments of the effect of each modality separately, and the problems involved in attempts to obtain such estimates include length bias, lead-time bias, self-selection, and many other factors (1-3). We do not know, therefore, how much mammography contributed to the good results from screening older women. We can conclude, however, that mammography was not beneficial to women age 50 and younger, because even the three modalities together did not seem to be helpful.

The H.I.P. study used the radiologic techniques of the early 1960's, and significant technical advances have been made since then. The most modern equipment, properly used, can produce distinctly better images now than then so that detection of more lesions at earlier stages is possible. However, no data are available to determine by direct means whether this earlier detection is beneficial for women age 50 and younger. All of the evidence is indirect. Much of it depends on the assumption that breast cancer in women over 50, essentially all postmenopause, is the same disease in all important biologic respects as is breast cancer in younger women. This assumption may well be false. Whereas breast cancers in these two age groups tend to have the same morphologic expressions, they differ substantially in epidemiologic features, hormonal and biochemical concomitants, response to treatment, and other

BEST COPY AVAILABLE

factors. Thus we cannot ignore the fact that the H.I.P. study, the only reliable source of data on the long-term effects of breast cancer screening, produced entirely negative results for women under age 50. (Large-scale studies with modern mammographic equipment are now or soon will be in progress in the Netherlands, Sweden, and perhaps Canada. Their results, when available, may modify present conclusions.)

With respect to the radiation risks of mammography, again no direct evidence exists. There are simply no data on the long-term followup of women exposed to X-radiation of the same dose level, beam quality, and fractionation pattern as that used in breast cancer screening. Most of the arguments have centered on whether the dose-response relationship is linear; that is, whether the likelihood of causing breast cancer is in direct proportion to the total amount of radiation absorbed. I believe that the linear model should be used for doses up to several hundred rads, although some people (including many radiologists) believe that it overstates risks, and others (including radiation biologists and others) believe that it understates risks. The linear model for X-ray carcinogenesis in the breast should be regarded as a "best estimate", not a "conservative" model, for three reasons: 1) it fits all available data (14-17) very well, 2) it has a direct interpretation in terms of present understanding of cellular and molecular events in radiation carcinogenesis, and 3) it avoids the unnecessary "looseness" and complexity of models with larger numbers of fitted parameters. That the survivors of the atomic explosions in Japan have had a distinct elevation in the incidence of breast cancer after exposere to just 17 rads is significant.

Application of the linear model requires some knowledge of the radiation doses used in the practice of mammography. These have varied widely, with occasional reports of extremely high doses (2,3). Radiation doses in mammography need to be quite high (even with "low"-dose methods) because of the small differences in radiographic density among fat, fibrous and glandular tissue, and masses of malignant cells. In the United States, the average midbreast exposure for a complete examination (2 films/breast) may have been in the range 3-5 rads at the time of the H.I.P. study. Over time, and with the partial shift from early methods to xeromammography, average doses declined to perhaps 1-2 rads by the summer of 1975. At that time public and professional awareness of the radiation hazards in mammography increased rapidly. As a result, a sharp acceleration occurred in the move toward low-dose methods, and film-screen combinations were much more widely used. Also, the degree of caution and control over the use of existing equipment increased. Average midbreast exposures for a complete examination may now be about 0.5 rads in the United States (18) and further significant reductions are likely as more hospitals and clinics adopt improved techniques. This recent rapid drop in average exposure was due mostly to public pressure and should be regarded as one of several beneficial effects of extensive coverage of the subject by general newspapers, magazines, radio, and television.

Radiation risks are not the only health hazards of breast cancer screening. Other authors have commented on the high frequency of negative biopsies, on surgical mortality, and on other matters [see e.g., (19-20), and (21) with following discussion]. Some of the research needs on radiation risks have been described by Dethlefsen et al. (22).

BEST COPY AVAILABLE

As discussed above, data about the risks of mammography are not entirely satisfactory, while no data exist to show benefits in women under age 50. Just these two points provide reason to be cautious in the use of mammography to screen asymptomatic young women from the general population. Two additional problems make the broad-scale, indiscriminate, use of mammography before the age of 50 distinctly unwise. These problems are the overdiagnosis of "cancer", and the likelihood of synergism between radiation and other risk factors.

The first of these problems, overdiagnosis, has also received extensive public exposure in the United States, especially during late 1977 and early 1978. A group of 27 large demonstration centers for breast cancer screening had reported a total of 1,810 "cancers" found during a series of examinations of about 280,000 women. Five hundred ninety-two were described as "minimal cancer" (a term I deplore). A group of eminent pathologists examined slides for 506 of these minimal cancers and concluded that 66 were entirely benign, 22 were noninvasive but could not definitely be classified as benign, and 262 were considered noninvasive neoplasms (23). Thus there was no evidence that 350 lesions, or 70% of the "cancers" reviewed by this group, presented any real threat to life and health. This fact is particularly significant because the promoters of mammography have given great emphasis to the "minimal" cancers as showing that screening can detect cancers at an early stage. Unfortunately, news articles for both public and professional readers failed to distinguish between two distinct kinds of mistakes: whether the pathologist made an error in diagnosis, and whether the surgeon made an error in clinical judgment. The former is most important in evaluating the overall impact of a large public screening program; the latter is most important in the management of individual patients. Thus statements [see, e.g., (24)] that there were only three clear errors, not 66, depends on a large number of doubtful assumptions, including the blanket assumption that there was no error in any case in which biopsy and mastectomy were performed as separate surgical procedures. This assumption was presumably made because a two-stage approach allows examination of permanent as well as frozen sections, but surely, the same mistake made twice is still a mistake. The pathology review group stands by its original opinion on each of these 66 benign lesions, except for two cases in which the original classification was ascribed to "computer error" and 16 in which the classification as "benign" led to the submission of additional slides that were claimed to be from the same patient (25).

This is a serious matter, but more serious is the large group of noninvasive neoplasms (262 of the 506 lesions reviewed). We simply do not know what proportion, if any, of these neoplasms will ever progress to the more usual forms of breast cancer that invade, metastasize, and kill. That some do is likely, but recent work indicates that the proportion must be small. For example, Lattes (26) has reported on a series of 210 patients with lobular noninvasive neoplasms incidentally detected. Seventeen percent had developed invasive cancers after an average of 7-8 years of observation, but half were in the breast contralateral to the lobular lesion. Others (27-30) have also noted a relatively low frequency or rate of incidence of invasive cancer following the detection of noninvasive neoplasms, although results have differed on whether lobular or ductal lesions present a greater long-term hazard. At present we do not know whether and how to treat such lesions. Answers to these questions will depend in part on the development of a better understanding of the multicentric origin of many breast cancers, including those found at early stages by screening (31-32).

With respect to the likelihood of synergism between the carcinogenic effects of radiation and the effects of other risk factors, we again have no data. However, the fact that carcinogenic agents are generally synergistic in laboratory animals is widely accepted, and good evidence demonstrates synergy in some human cancers. For example, the relation between lung cancer and cigarette smoking is very much magnified by exposure to either asbestos (33) or radiation (34). At least two other studies are in progress to determine whether radiation is synergistic with other causes of cancer in the human female breast, but that work is not yet complete (Boice at this symposium, and 35).

If a significant degree of synergy exists, of course, women at high risk of breast cancer should be actively excluded from general x-ray screening programs. This contrary to current practice in the United States and elsewhere, and we may in time come to regret the present emphasis on preferential screening of women who are at especially high risk of developing breast cancer.

Generally, to assess the impact of risk factors taken one at a time is very difficult, even without the complications of synergism. Recent work on the implications of fibrocystic disease has generally suggested a modest elevation in risk of breast cancer (36, 37), family history is important (38), but no good evidence supports the idea that cancer incidence is correlated with the size of the breast, which is largely composed of fat and supporting tissues [see, e.g., (39)]. Suggestions that fibrocystic disease may be associated with cancers having a favorable prognosis (40) cannot yet be confirmed or denied. Several authors (41-43) have developed models for estimating the effects of two or more risk factors in combination, but those models need much testing and further development before they can be applied with confidence to estimate risks for specific individuals. Kessler (44) has considered some of the broader issues in identifying high-risk population segments for special attention in screening programs.

An additional point should be considered in discussions of breast cancer screening for women under age 50, although it is a problem in the use of screening results instead of in the screening itself. One justification for the periodic examination of young women has been the value of providing reassurance to most screenees that breast cancer is not present. Unfortunatley, not all cancers are detectable at screening, and this problem is particularly acute in young women because the denser breast tissue makes radiologic examination more difficult. Several reports [see, e.g., (45)] have shown that mammographic screening of young women has more often led to a significant delay in diagnosis than it has advanced the date of cancer detection. To the extent that screening programs are used to provide reassurance, this problem of false-negative results will continue to be a serious one.

In the United States, many radiologists would like to give every woman one or two so-called "baseline mammography studies" at ages 35-40 (46). Two reasons have been advanced. The first is to have the films on file for comparison with later X-rays, if any should be taken. That would be of value only if the use of baseline films really changes the interpretation of later results in a significant proportion of cases. Colleagues who are radiologists tell me that baseline films can provide welcome reassurance that later films have been correctly interpreted, but that they rarely affect the final diagnosis or the management of patients.

The second reason given for baseline mammography is to identify from the appearance of the breast parenchyma a small subgroup of women who are at especially high risk of breast cancer. This argument is based primarily on the work of Dr. John Wolfe (47, 48), who has reported very impressive results. However, other radiologists (49-54) have had very limited success in duplicating those results in well-controlled studies. Thus, to recommend baseline mammography seems unwise unless Wolfe's classification can be refined and improved for general application.

There is a large and expanding literature on newer techniques of mammography, on radiation exposure levels with various techniques, and on methods of quality control. That literature will not be reviewed here, except for brief comment on a few recent reports that illustrate important points. Several authors [e.g., (55,56)] believe that a single view is sufficient for screening mammography. There is widespread concern, and some evidence, that breast cancer screening often fails to meet minimum quality standards for both radiologic (57,58) and clinical (3) examinations. Much active research is in progress on the development of entirely new imaging systems and on new ways of using present systems [(59), and several chapters in (60)].

These and many other questions about breast cancer screening have been examined by a long series of committees. Perhaps it should not be surprising that committees composed primarily or exclusively of radiologists have generally advocated vigorous promotion of mammography with loose control and a low age limit for starting periodic examinations. Committees with a more balanced membership, including surgeons, pathologists, epidemiologists, radiation biologists, and persons from other relevant disciplines, in addition to radiologists, have come to different conclusions. Recently, five such committees (4, 23, 61-64) have arrived at nearly identical conclusions with respect to the appropriate role of mammography. The most recent report (64), which drew in part on the others, was summarized by Thier (65) as follows:

> "It seems reasonable to screen women over 50 years of age with a combination of physical examination and X-ray mammography. Mammographic equipment should be well calibrated, and the dose of radiation should be less than 1 rad. The patient should ask for and keep a record of her radiation exposure. Women under 50 may continue to be screened by physical examination, but should be screened with X-ray mammography only if they have already had breast cancer or if they are between the ages of 40 and 49 and have a mother or sister who has had cancer of the breast. Though the risk from X-ray mammography may be small, it is finite, and must be balanced against the absence of any demonstrable benefit from screening women below 50 years of age. When screening is done, it should probably be on a yearly basis. Lesions of less than 1 cm should be evaluated by more than two pathologists

> before any definitive operation is performed, and before a firm diagnosis of cancer is reported to the patient."

For reasons implied above, I endorse those guidelines. I do have some reservations about them, also outlined above, but basically I believe these guidelines to be both reasonable and defensible. They were recently adopted as official policy in all agencies of the U.S. Government (66). In one large screening program, approximately 17% of women aged 35-49 years actually attending the screening clinic qualified for mammography under guidelines very similar to these (67). These guidelines apply only to screening, that is, to the examination of women who do not have signs or symptoms that specifically suggest the possibility of breast cancer. Strax (68) and Lester (69) have summarized the views of persons advocating less restrictive guidelines.

I hope that other groups in other nations will examine the matter with equal care before launching breast cancer screening programs that may be either too broad or too narrow.

REFERENCES

(1) BAILAR JC, Ann Int. Med. 84 (1976) 77.
(2) BAILAR JC, Cancer 39 (1977) 2783.
(3) BAILAR JC, Clin. Ob. Gyn. 212 (1978) 1.
(4) UPTON AC, et al., J. Natl. Cancer Inst. 59 (1977) 481.
(5) MORGAN KZ, Science 195 (1977) 344.
(6) BROWN H, Science 195 (1977) 348.
(7) ROSSI HH, Rad. Res. 71 (1977) 1.
(8) ELKIND MM, Rad. Res. 71 (1977) 9.
(9) WITHERS HR, Rad. Res. 71 (1977) 24.
(10) BROWN JM, Rad. Res. 71 (1977) 34.
(11) UPTON AC, Rad. Res. 71 (1977) 51.
(12) MOLE RH, Meeting of British Breast Group, 17 Feb. 1978.
(13) SHAPIRO S, Cancer 39 (1977) 2772.
(14) BOICE JD, MONSON RR, J. Natl. Cancer Inst. 59 (1977) 823.
(15) SHORE RE, et al., J. Natl. Cancer Inst. 59 1977) 813.
(16) MCGREGOR DH, et al., J. Natl. Cancer Inst. 59 (1977) 799.
(17) BARAL E, Cancer 40 (1977) 2905.
(18) JANS R, personal communication, 1 Mar. 1978.
(19) COATES HR, Am. J. Surg. 134 (1977) 77.
(20) SCHNEIDERMAN MA, AXTELL LM, Surg. Gyn. Ob., in press.
(21) LEWIS JD, Ann. Surg. 184 (1976) 253.
(22) DETHLEFSEN LA, et al., unpublished report Nov. 7, 1977.
(23) BEAHRS OH, Yale Journal, in press.
(24) Cancer Letter 4 7 (1978) 2.
(25) MCDIVITT RW, personal communication, 1 March 1978.
(26) LATTES R, Cancer, in press.
(27) FISHER ER, FISHER B, Ann. Surg. 185 (1977) 377.
(28) PAGE DL, Submitted for publication, 28 Feb. 1978.

(29) TOKER C, GOLDBERG JD, Path. Ann. (Part 1) 12 (1977) 217.
(30) BETSILL WL, et al., presented at Int. Acad. Path. 7 March 1973.
(31) LAGIOS MD, Cancer 40 (1977) 1726.
(32) PATCHEFSKY AS, et al., Cancer 40 (1977) 1659.
(33) SELIKOFF IJ, et al., J. Am. Med. Assoc. 204 (1968) 106.
(34) LUNDIN FE, et al., Health Physics 16 (1969) 571.
(35) MILLER A, personal communication, 22 Nov. 1977.
(36) MONSON RR, et al., Lancet 2 (1976) 224.
(37) NOMURA A, Am. J. Epid. 105 (1977) 505.
(38) ANDERSON DE, Cancer 34 (1974) 1090.
(39) ROBERTSON AJ, Brit. Med. J. 1 (1977) 1283.
(40) BERNSTEIN TC, J. Am. Med. Assoc. 238 (1977) 345.
(41) FAREWELL VT, Cancer 40 (1977) 931.
(42) DAVIES DF, et al., to be published, J. Natl. Cancer Inst.
(43) VAN DER LINDE F, Schweiz. Med. Wschr. 107 (1977) 962.
(44) KESSNER DM, J. Commun. Health 1 (1976) 216.
(45) RESNICK CJ, J. Am. Med. Assoc. 237 (1977) 967.
(46) Bulletin, Am. Coll. of Radiology 32 8 (1976) 1.
(47) WOLFE JN, Cancer 37 (1976) 2486.
(48) WOLFE JN, Radiology 121 (1976) 545.
(49) PEYSTER RG, et al., Radiology 125 (1977) 387.
(50) EGAN RL, MOSTELLER RC, Cancer 40 (1977) 2087.
(51) MENDELL L, et al., Am. J. Roentgenol. 128 (1977) 547.
(52) WILKINSON E, et al., J. Natl. Cancer Inst. 59 (1977) 1397.
(53) MOSKOWITZ M, et al., Breast 3 (1977) 37.
(54) RIDEOUT, DF, POON PY, Breast Cancer Symposium, Madison, 6 Nov. 1976.
(55) LUNDGREN B, JAKOBSSON S, Cancer 38 (1976) 1124.
(56) LUNDGREN B, Brit. J. Radiol. 50 (1977) 626.
(57) HUPPE JR, SCHNEIDER H-J, Radiologe 17 (1977) 197.
(58) PRESSMAN PL, Am. J. Surg. 133 (1977) 702.
(59) SMITH KT, et al., Radiology 125 (1977) 383.
(60) LOGAN WW (Ed.), "Breast Carcinoma - The Radiologist's
Expanded Role," Wiley (Toronto), 1978.
(61) BRESLOW L, et al., J. Natl. Cancer Inst. 59 (1977) 467.
(62) BRESLOW L, et al., J. Natl. Cancer Inst. 59 (1977) 473.
(63) THOMAS LB, et al., J. Natl. Cancer Inst. 59 (1977) 495.
(64) THIER SO, et al., Yale Journal, in press.
(65) THIER SO, New Engl. J. Med. 297 (1977) 1065.
(66) Federal Register 43 (1978) 4377.
(67) FINK DJ, personal communication, 1 Dec. 1977.
(68) STRAX P, Consensus meeting, NIH, 14 Sept. 1977.
(69) LESTER RG, Consensus meeting, NIH, 14 Sept. 1977.

ATTACHMENT 2

Associate Director, PPA
: Director, National Cancer Program, NCI

March 21, 1973

Deputy Associate Director for Cancer Control, NCI

Breast Cancer Detection Demonstration Units

1. I believe you have seen the memorandum I sent to the Director, DCBD, on March 1, 1973 and the plan to call on your office for assistance in obtaining an independent epidemiological study of the Breast Cancer Demonstration Center project. This memorandum is to provide you details on the points that should be covered in your review.

2. The program is concerned with several aspects of breast cancer, reflecting in varying degrees the different uses of mammography:

a) Screening of asymptomatic populations as a tool in the earlier detection of breast cancer,

b) Diagnostic work-up of patients that come to medical attention because of suspicious signs or symptoms,

c) Specimen radiography as minor aid to case management, and

d) Research on the natural history of breast changes, especially those related to malignant neoplasms.

At present, the Cancer Control Program is most concerned with the first two of these. Since they may have quite different implications with respect to project size and design, they should be considered separately as well as together in your review.

3. In the attachment I have listed a number of questions under three headings:

a) General

b) Screening

c) Diagnostic work-up

I believe the attachment is self-explanatory except perhaps for definitions of "Service" and "Demonstration." By "Service" I mean the provision of a screening technique solely because of its value to the participants when it is delivered in this kind of program, in this way, at this time. By "Demonstration" I mean demonstration to the medical community and/or the general population of what this technique can do for them, with the

BEST COPY AVAILABLE

expectation that they will use the technique on a wider and wider scale after the demonstration is concluded. Demonstration, as defined, explicitly excludes research to determine whether some technique is of value, a function of other NCI Divisions. I do however want to assure that NCI makes maximum use of the research opportunities inherent in service and demonstration programs that are supported by CCP for other reasons. For this reason the attachment refers to a few research-related questions.

4. As you may know, there were no formal RFPs developed for this project, since the initial work necessary to stimulate the proposals was done by units of the American Cancer Society. Attached for your information, however, are Project Information and Workscope documents, and also the RFP which was developed by NCI on the supporting Statistical Center.

5. I would appreciate your reviewing the attached questions and addressing yourself to the matter of what would be involved in developing acceptably complete answers to these questions.

6. This is important. NCI and ACS have already announced the selection of the first three centers, and we must get them started almost immediately. There is considerable outside interest in this program, and I have already received numerous inquiries about delays.

7. I would welcome the opportunity of discussing this matter with you.

John C. Bailar, III, M.D.

Attachments

cc:
[illegible]:ga 3/31/73
Dr. Olson

BEST COPY AVAILABLE

CCP
(3/21/73)

Attachment
Questions for Study
Breast Cancer Detection Demonstration Units

I. General Remarks

Why is NCI supporting the breast cancer detection program as a demonstration program and out of CCP funds? Is our objective that of having a large proportion of women in the United States over the age of 35 undergo annual mammography, or annual mammography plus history and physical examination? If so, a number of specific questions need to be answered. They can be summarized as four more general questions:

a) How good is the evidence that mammography is in fact effective in reducing cancer mortality or disability?

b) Is the present program designed in an optimum fashion to reach the objective stated above?

c) How much are matters of cost likely to interfere with widespread use of mammography (i.e. beyond the demonstration program)?, and

d) Is there good reason to think that a large proportion of women in this Country will voluntarily go through this procedure? Past experience with vaginal cytology is not encouraging, though cytology is less expensive, perhaps more effective in percentage terms, and, for the women concerned, significantly less troublesome than mammography.

II. Basic Questions

What criteria should be used to judge the success of the overall program? The success of each unit separately? Under what conditions should support of an unsuccessful unit be terminated?

How long should NCI plan to support annual screening in this program? How long should NCI plan to continue subsequent follow-up?

Can we reduce the amount of information collected on each screenee, or each positive screenee, without serious loss?

Are the proposed overall size and cost of the program reasonable in relation to the various objectives and the likelihood of success of each objective? Is the figure of 5,000 new asymptomatic screenees per year per center optimal?

BEST COPY AVAILABLE

Attachment Page 2

III. Screening

A. Service. How strong is the evidence that mammography is a useful tool in the earlier detection of breast cancer? How much does mammography add to the benefits of regular examination by history and physical? What is the estimated effect of this earlier detection on breast cancer mortality and disability, and how good is that estimate?

How strong is the evidence that a 1-year interval between examinations is optimal? Is a single fixed interval appropriate for all patients?

Are the target populations optimal? Should there be a lower age limit, and if so what age? Should factors of risk (other than age) be used as criteria for screening?

How much does a mammography screening program raise the frequency of biopsy and other diagnostic procedures, particularly the frequency of negative biopsy? What is the morbidity and cost of these additional procedures in relation to the yield of early cancers found? Is there reason for concern over the effects of repeated radiation exposure?

Are the proposed follow-up mechanisms adequate to assure that every positive or suspicious lesion detected is promptly investigated and treated?

In general, what are the expected benefits and expected costs (in the broadest sense) of widespread use of mammography and other screening techniques for asymptomatic populations?

B. Demonstration. What is the program designed to demonstrate, to whom, with what ultimate effect? What is the likelihood that this demonstration program will lead to wider use of mammography, alone or in conjunction with other detection measures? What should be done to improve the effectiveness of this program as a demonstration activity? What are the problems in getting mammography more widely accepted in screening, by health professionals and by the public? Is the present program likely to reduce these problems?

Are the target populations optimal for demonstration purposes?

How much are economic factors likely to affect the use of mammography as a screening device, at present cost levels and at levels that might be attained (e.g. using thermography as a pre-screener; preliminary readings by non-physicians)?

Is the goal of 5,000 new patients per year the optimum size for each demonstration program? What is the likelihood that it will be attained in each center?

BEST COPY AVAILABLE

C. Research. What are the research objectives of the program with respect to population screening, and should they be expanded, reduced, orfurther refined? What is the likelihood that those objectives will be attained with the present program size and design, or with a modified program?

Are the data likely to be sufficiently complete and sufficiently accurate for research purposes (e.g. data on reasons for seeking screening; data on treatment and outcome of cases detected; data on cancers missed by the screening program)? Should "saturation" screening be attempted in one or more areas?

D. Education. What are the probable educational effects on this program, on various segments of the general population and on various segments of the health profession? Can they and should they be improved, and if so how?

IV. Diagnostic Work-up

A. Service. How strong is the evidence that mammography is a useful tool in the diagnostic work-up of suspected breast cancer?

How often do the results of mammography directly affect decisions on patient management, especially decisions regarding biopsy? How often should they?

Should criteria be established for the use of mammography as a tool in diagnosis (as opposed to screening)? If so, what criteria?

B. Demonstration. What is the probable effect of this program in promoting the proper use of mammography as a diagnostic tool? Could that effect be significantly improved, and should it be?

C. Research. Does this program offer opportunities for research studies on the use of mammography in diagnostic work-up? If so, how should those opportunities be exploited?

D. Education. What are the probable educational effects of this program with respect to diagnosis of suspected breast cancer? Can and should these effects be improved, and if so how?

BEST COPY AVAILABLE

ATTACHMENT 3

Associate Director, PPA
Director, National Cancer Program, NCI

March 30, 1973

Project Officer
NCI-ACS Breast Cancer Demonstration Projects

Breast Cancer Detection Demonstration Units

Dr. Bailar's letter of March 21, 1973 is most disturbing to me.

The project objectives have been well spelled out in the "project information."

This project has limited objectives and they have been pretty much dictated by the American Cancer Society. In summary they are:

Can American Cancer Society volunteers mobilize a large number (100,000 per year) of volunteers for thermography, mammography, and a physical exam?

This rather ends the objectives and this means that the only statistically sound method of prolonging a disease free interval for cancer (i.e. the H.I.P. study) will be applied to a large population.

This in itself would be an interesting goal to achieve.

Why try to write research or controls into this ongoing program?

Kenneth B. Olson, M.D.
KBOLSON:ba:3/30/73

BEST COPY AVAILABLE

Reprinted from CANCER, Vol. 39, No. 6, June
1977. Copyright, © 1977, by the American Cancer
Society, Inc. J. B. Lippincott Company.
Printed in U.S.A.

ATTACHMENT 4

SCREENING FOR EARLY BREAST CANCER: PROS AND CONS

JOHN C. BAILAR III, MD, PHD

Health benefits and risks of breast cancer screening programs have been both criticized and defended. This paper summarizes and evaluates those arguments, discusses changes that have already occurred, and looks at prospects for further improvement. Early detection of breast cancer can undoubtedly reduce mortality. X-ray mammography also undoubtedly carries a risk of causing breast cancer at some future time. Both benefits and risks can be estimated. In terms of breast cancer mortality, adding mammography to a program of annual breast examinations of average U.S. women is questionable for women under age 55 but likely to be beneficial for older women. However, the break-even point is closely related to the average radiation exposure of breast tissue, and might be as early as age 50 in a few centers now using optimum techniques and equipment. For women with below-average risks of breast cancer the age would be higher, and for a few women with a high probability of developing breast cancer it would be lower. The break-even point should be significantly exceeded before mammographic screening becomes worth the time, trouble, and other costs. Breast cancer screening programs have been improved significantly since criticisms were first publicized in mid-1975. Partial improvements include reduction in radiation exposure (at least in some centers), guidelines from the National Cancer Institute (NCI) and the American Cancer Society (ACS) for restricting the screening of women under 50, and changes in the patient consent form signed by screenees in the NCI-ACS program. There has been a rapid and marked increase in both professional and public awareness of the need to balance the benefits of screening with its risks and costs. Future improvements should further define the optimum design and application of breast cancer screening programs.

Cancer **39:2783–2795, 1977.**

THE FIRST RUSH OF UNINHIBITED, UNINFORMED enthusiasm for breast cancer screening has passed, permitting more sober evaluation of the pros and cons of various screening programs and modalities. Health benefits and risks of present programs have been both criticized and defended. This paper summarizes and evaluates those arguments, discusses changes that have already occurred, and looks at prospects for further improvement.

This analysis centers on the good and bad aspects of adding mammographic screening to periodic screening by physical examination and medical history alone, with particular reference to the periodic screening of asymptomatic women. Most women have minor breast symptoms at some point. "Asymptomatic," as used here, means "not presently having physical signs or symptoms that would require biopsy if mammography were unavailable." By this definition, asymptomatic refers to almost all of the population and includes many women who presently have minor or chronic symptoms thought to result from benign conditions.

The major premises of the analysis are:

(1) Evidence is conclusive that annual screening (history, physical examination, and mammography) can reduce short-term (less than 10 years) breast cancer mortality in women 50 years and older at the time of screening, but the precise contribution of mammography to this reduction is not clear.

Presented at the Conference on Breast Cancer: A Report to the Profession, sponsored by the White House, the National Cancer Institute and the American Cancer Society, November 22-23, 1976, Washington, DC

From the National Cancer Institute, Bethesda, MD

Address for reprints: John C. Bailar, MD, PhD, National Cancer Institute, Room 2A-09, Blair Building, Bethesda, MD 20014

I am indebted to Mrs Gertrude Anthony and Mrs Phyllis Jay for help in the preparation of this paper

Accepted for publication January 26, 1977

(2) The size and distribution of radiation hazards should be carefully examined. Available data are adequate to do so. I disagree with the philosophy that risks do not exist until they have been conclusively demonstrated.

(3) The number of cancers discovered does not directly measure the value of screening, which also depends on survival in the absence of screening, deaths that occur despite earlier detection, self-selection of screenees, and unavoidable biases in results.

(4) Mammography must be evaluated as one among several useful screening modalities; individual screening examinations must be judged in the context of lifetime patterns of screening; and the likelihood of failures of physicians and screenees to follow recommended practices must be considered

(5) The most important end-point for evaluating cancer screening programs is overall reduction in the number of deaths from cancer. Total years of life is a reasonable alternative measure and has been considered by some other authors.[14,18,61] The latter measure gives less weight to the prevention of cancer deaths in older women than in younger ones. The proper choice between these measures depends on whether screenees (not their physicians or other persons) are more concerned about cause of death or length of life; women I have talked with have tended to emphasize the former.

(6) There is no adjustment for the fact that radiation-induced cancers might be subject to early detection in subsequent screening examinations. Other analyses have included this factor.[14,18,61] However, I object to the implications that, first, it is all right to cause cancer if it can be cured later; and second, women who once enter a screening program should be expected or required to continue indefinitely so damage already done will be detected.

Risks of X-Ray Mammography

What are the direct risks of screening? Among screening modalities now in general use, medical history, physical examination, and thermography are entirely safe. The only appreciable hazard is from x-ray mammography.

Evidence is abundant from both human (see review in[46]) and animal studies that x-radiation is carcinogenic to breast tissue. Unfortunately, there are no data on the effects of radiation of just the frequency, dosage, and physical parameters used in mammography. Some extrapolations, which I believe can be made reliably, are necessary. These involve the shape of the dose-response curve (linearity and threshold), effects of dose rate and dose fractionation, energy level of incident radiation, and effects of exposing persons at different ages.

The shape of the dose-response curve for radiation carcinogenesis at low radiation doses has been well discussed. It is sometimes stated or implied that such curves are nonlinear and that a threshold may exist below which exposure is entirely (or almost entirely) safe.[5] This philosophy has been best expressed by a report of the National Council on Radiation Protection and Measurements (NCRP).[37] Unfortunately, that report is only a philosophical discussion and includes no data, which are obviously essential to any resolution of the question. It is also unfortunate that the NCRP report did not offer specific alternatives to the linear model, nor did it give bounds within which linearity was considered a close approximation to reality.

Brown,[12] who considered dose-response relationships for radiation carcinogenesis in general, concluded that linear extrapolation from doses up to 100 rads may underestimate risks at low doses. Brown also discussed possible mechanisms of radiation carcinogenesis and their relative importance. Morgan[36] and Ellett and Richardson[19] have dealt with the same problems, and Pochin[38] recently reviewed evidence that radiation doses less than 10 rads can be carcinogenic to human bone marrow, thyroid gland, and other tissues. Shellabarger[44] has summarized data showing that different forms of cancer display dose-response curves of markedly varying shapes. One consequence is that estimates of risk, including determination of the shape of the dose-response curve, must be based on observations on the organs or tissues of interest.

Only four sources of information seem suitable for assessing the shape of the dose-response curve for x-ray carcinogenesis in the breast. Relevant data are shown in Fig. 1. First, data from experiments by three laboratories on effects in the Sprague-Dawley rat[9,40,57] were summarized by Rossi and Kellerer,[42] who concluded that "in the case of x-rays, a linear dependence of incidence on dose appears to be consistent with the data." They also noted, however, that "even if the dose-effect relation for x-rays were in

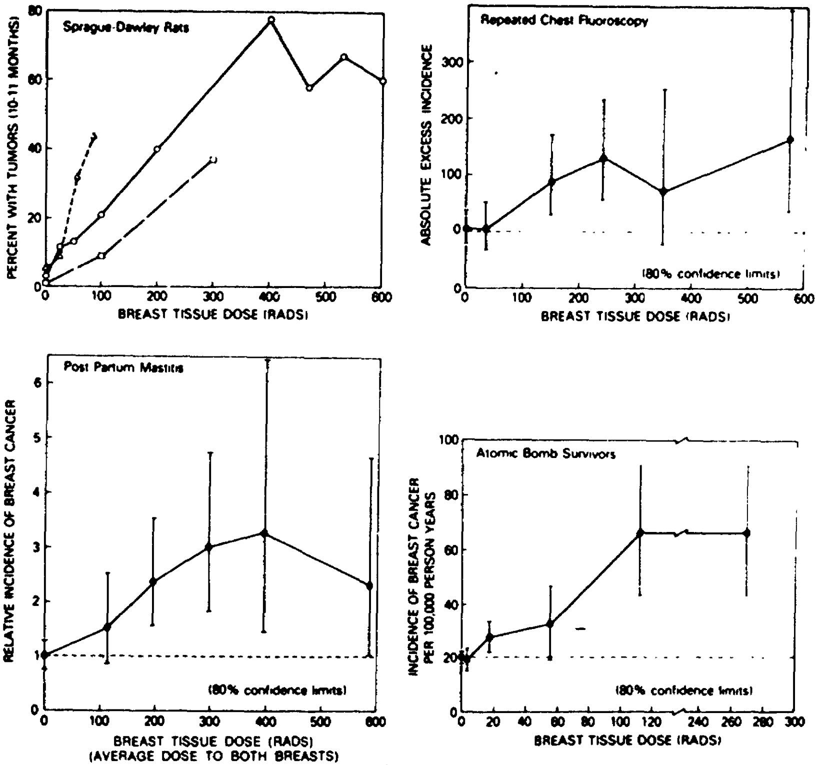


FIG. 4 Dose-response curves for radiation carcinogenesis in the breast Sources (Top left) ○ Bond *et al*[8] △ Shellabarger *et al*[60] Vogel and Zaldivar[67] (Bottom left) Shore *et al.*[58] (Top right) Boice and Monson[7] (Bottom right) McGregor *et al*[33]

fact linear in the dose range investigated (a distinct possibility in view of the limited accuracy of the experiments), the linearity must be accidental and there is no justification for a linear extrapolation." Figure 1 repeats data from one source of Rossi and Kellerer, while data from the other two laboratories have been updated from more recent publications. These data show a remarkable agreement with a linear nonthreshold effect down to the lowest dose examined, 25 rads. These data support a linear relationship better than they support any alternative.

The second source is the long-term follow-up of survivors of the atomic bombs in Hiroshima and Nagasaki.[33] No significant difference in the incidence of breast cancer was found between Hiroshima (significant neutron radiation) and Nagasaki (largely gamma radiation), so results for the two cities have been pooled. No increased risk is evident at the lowest point reported (2.9 rads), though standard errors are relatively large. The increase at 17 rads is distinct, and all remaining points appear to be in good conformity with a linear nonthreshold effect.

Third are observations on women who had repeated fluoroscopies during therapeutic pneumothorax for tuberculosis.[7] Again, a linear, nonthreshold dose-response curve is suggested except possibly for the lowest point, where the standard error is large enough to leave some doubt about the risk. Other reports on women subjected to repeated pneumothorax are fully consistent with this figure but do not lend themselves to estimation of the dose-response curve.[7]

The last data source is a recent report on women subjected to radiation treatment for postpartum mastitis.[40] Once more the carcinogenic effect is in good conformity with the linear model through the lowest dose observed, 100 rads.

Other sources of human data have suggested an increased risk of breast cancer after radiotherapy for other cancers[38] or for hirsuitism or acne of the skin of the chest,[32] but the data cannot be used for the estimation of the dose-response curve.

Three of the four dose-response charts show evidence of a flattening or even decline at the highest doses, such that linear extrapolation from high doses would underestimate risks. This well-known effect is commonly attributed to sterilization or even outright destruction of the target organ, so that few cells are left to become malignant.

This brief review exhausts the store of scientific data bearing directly on the dose-response curve for radiation carcinogenesis in the human breast In summary, a long philosophical discussion concludes that the linear nonthreshold model may overestimate risks at low radiation doses, a more recent survey concludes that the opposite may be true, and all available data sources are consistent with a linear nonthreshold effect. Thus the linear model is not only plausible· the data suggest no reasonable alternative. Many radiation effects are nonlinear (e.g., erythema, epilation, tumor destruction during radiotherapy, even the induction of some forms of neoplasms[40]), but evidence is now sufficient to accept the linear model for estimating low-dose carcinogenesis in the breast, at least until someone produces data to the contrary.

While a linear nonthreshold response agrees with available data, additivity of the effects of fractionated doses is less certain. Radiation exposure in long-term mammography screening programs is fractionated, with a small incremental dose at evey examination. Some laboratory data suggest that fractionated exposure of rodents to a high total dose may produce cancer just as effectively as a single dose of the same size, whereas other data show opposite results.[37,43,60] Most data are based on experiments with rodents, and little or no evidence exists that fractionation changes carcinogenic effects in human beings or other large mammals. There seem to be no completely appropriate research studies on the kind of fractionated exposures characteristic of mammography screening programs, though the fluoroscopy series is close. However, it is commonly agreed that a protective effect (if any) of fractionation or dose-rate reduction is particularly relevant to exposures in dose ranges well beyond those characteristic of mammography.[37] Thus I have assumed that effects are additive.

Next, I have assumed that the energy level of the x-rays is irrelevant except as it affects the density of ionization, measured in rads. This hypothesis is generally accepted by radiation biologists, and I know of no data to the contrary.

Finally, I have assumed that radiation risks are independent of age at time of exposure. Some of the data cited above suggest that the risk is especially high at ages under 35 and declines with advanced age, but this finding must be confirmed and extended before it can be used in assessing the impact of screening programs.

In adopting the model of radiation carcinogenesis described here, I have found the experience of the atomic bomb survivors especially convincing, not only because an effect was observed with only 17 rads, but also because this observation was in a human population with an unusually low "natural" incidence of breast cancer. It is true that these women were exposed to a single, sharp dose of ionizing radiation, but a tissue dose of 17 rads is within the range of exposures reported for a *single set* of mammographic studies, and many clinics[5] might deliver a total dose of this size in just a few examinations. Of course, there is nothing special about 17 rads; that is just the point at which we now have data demonstrating a risk. Does the risk begin at 16 rads, or 15, or one, or zero? Available data suggest to me that it begins at zero.

That mammographic studies cause human breast cancer has not, of course, been directly demonstrated. Such direct evidence is unlikely despite a substantial radiation risk. First, it is impossible to distinguish by clinical or pathological means between cancers induced by radiation and by other factors; we simply cannot say that one breast cancer was caused by mammography and another was not. Further, we do not have long-term observations on large numbers of women subjected to numerous mammographic studies. Large populations would have to be followed for at least 20 years (assuming a latent period of about 10 years), and mammography was uncommon 20 years ago. Finally, even a large population would be unsuitable unless problems of self-selection and other biases could be overcome, a requirement that may be impossible to meet. Certainly, many women who had mammography 10 or more years ago have subsequently developed breast cancer, but no one can say just which ones were caused by the radiation and which would have occurred anyway.

While direct proof of risk by long-term follow-up of women in mammographic screening programs is unreasonable to demand, the available evidence is reliable, convincing, and in my view conclusive. Critics of the linear nonthreshold additive model must now assume the burden of proof that this model seriously overstates risks at low doses. At this point, any alternative to the linear model is pure speculation.

Radiation Doses in the Real World

Discussions of radiation exposures in mammography have been complicated and confused by frequent failures to distinguish among important factors. Examples include the differences among or between 1) roentgens and rad; 2) air doses, skin doses, surface doses, and tissue doses; 3) doses from a single exposure, from a "standard" set of films, and from a standard set plus additional films (repeat films, extra views, etc.); and 4) attainable doses, current optimum doses, average doses, and the upper range of doses actually need.

Further, until recently, accurate dose information has been very difficult to obtain because of technical limitations on the more common types of radiation dosimeters.

For the first three items above, the most useful single parameter is the total ionizing radiation (rads) delivered to the "average" breast cell (mean tissue dose) during a single screening examination (standard set plus any additional films). In past years, the standard set often included three films of each breast; some mammographers now believe[15,30] that one film of each breast is sufficient for screening purposes, though others believe further work is needed.[30] The usual practice today is to use two films of each breast and to take additional films when indicated. Moskowitz[34] reported an average of 5.5 (both breasts, or 2.75 per breast) exposures in a clinic where two films per breast was standard procedure. In the absence of broader data, that is the figure used below.

The tissue dose at 2 cm is approximately 21% of the surface dose (in rads) and about 12% at 3 cm.[55] The midbreast region may be about 3.0 cm from the surface when moderate breast compression is used.[13] However, because attenuation of dose is nearly exponential from entrance to exit, and because the entrance dose is commonly greater for thick breasts than for thin ones, the mean tissue dose is higher than the midbreast dose. My own estimates are that the tissue dose, averaged 1) through each breast, and 2) for breasts of different thickness, is about 22% of the surface dose.

Finally, the air dose in roentgens is very close to the skin dose in rads. Thus each roentgen of air dose in a single exposure is approximately equivalent to 2.75 × 0.22 = 0.605 rads mean tissue dose for a complete film set.

Only two broad-scale sources of data exist on doses actually delivered during mammography. First are reports[41,42] on radiation exposures in the 27 Breast Cancer Detection Demonstration Programs (BCDDPs) jointly supported by the American Cancer Society (ACS) and the National Cancer Institute (NCI). These data show a single-exposure air dose, averaged over 63 mammographic systems, of 3.1 R in the first year of the program. By the second year the average (now over 57 systems) was 2.2 R, a reduction of 29%. However, the most active detection center in the program still delivered an average of 4.93 R, and one center went as high as 5.5 R.[41] Indications are[43] that the latter has been significantly reduced since Malone's report.[41] The 2.2-R average is equivalent to about 2.2 × 0.605 = 1.33 rads average tissue dose per complete examination.

These dose levels, obtained in a carefully monitored, tightly controlled demonstration program, are probably the lowest that one could expect at present for any broad multi-center screening activity. Wochos and Cameron[60] have discussed some of the problems encountered in a more general survey of patient exposures from diagnostic x-rays. Bicehouse[6] reported on exposure levels in 70 unmonitored screening clinics in Eastern Pennsylvania. The average single-exposure air dose was 8.2 R, but that average was heavily affected by five facilities that overexposed and underdeveloped images to deliver an average of 39 R and by an additional 11 facilities using a "high density" technique that delivered an average of 24 R. The highest single value reported was 47 R. Bicehouse has also noted[6] that some of the most extreme values were easily corrected on the spot and should not recur, so that average doses in that geographic area may have been significantly reduced since (and because of) his survey. There are reports[40,41] of at least four cases of radiodermatitis following mammography, indicating skin doses of hundreds of rads, but such doses are—we hope—quite unusual.

Women exposed to relatively high doses might return to the same clinic repeatedly, amassing huge total tissue doses, although they and their referring physicians might not have any direct indication that doses are excessive. Even mammographers themselves often do not know what dose they use, since nearly identical equipment and techniques often give markedly different exposures, and since many or most machines now in use have never been calibrated after leaving the factory.[33]

Jans[28] has reported the development of a program to monitor doses on a nation-wide basis. His results, based on a pilot study, are not yet available for full analysis. However, pilot results suggest that average doses are somewhat lower than in the Bicehouse survey and that extreme values are distinctly less common.

Image quality needs more investigation and public discussion. Dose reductions will clearly be unacceptable if the resulting radiographic images often fail to display cancers that would be visible at higher doses. In such situations it may be best to dispense with mammography altogether Malone[32] and Cameron* reported the beginning programs to assess image quality, but much remains to be done.

Benefits from Early Detection of Breast Cancer

My initial interest in the role of x-ray mammography was sparked not by a suspicion that the risks were high, but because the potential benefits seemed much lower than many people had been led to believe. What are those benefits?

Without doubt, earlier detection can reduce mortality. The best data on this come from a study by the Health Insurance Plan of Greater New York (HIP), which compared women invited to participate in a breast cancer screening program with those not invited.[47] Among 30,426 women in the study group, 70 had died from breast cancer within seven years of the initial round of screening; among a nearly equal number of matched controls, 108 had died. The observed difference is highly significant in both medical and statistical terms. However, the mortality difference is entirely limited to women at least 50 years of age; no difference was demonstrated for those under 50.[48]

Since findings in the HIP screening program were recorded independently for each of three screening modalities (medical history, physical examination, and mammography) the effect of each modality can be estimated separately. In the group invited for screening, 299 breast cancers were reported within five years of the start of the study, including 225 among the 20,166 women actually screened at least once. Over half of these breast cancers (132) were first detected by the screening examinations, but only 44 (15% of all breast cancers and 20% of those in screened women) would have been missed by omitting mammography from the initial and annual follow-up screens. This provides our best estimate of the number of breast cancers that can be found by adding mammography to a screening program of history and physical examination.

The key elements establishing the reliability of the HIP results are that: 1) women were assigned to the study or control group without reference to their risk of developing breast cancer or their current medical status; 2) the assignment was random; and 3) analyses of later mortality including consideration of women who refused screening as well as those who are accepted.

These aspects of study design and analysis avoid the two most important biases in results, the lead time bias and the length bias, as long as effects of the total screening program are considered. (They may reappear, however, if one attempts to isolate the effects of separate screening modalities.) Studies in which one or more of these elements is missing are subject to biases that may undermine conclusions.

Some have argued that the HIP study is out of date and that technical improvements in mammographic imaging permit detection of a higher proportion of cancers, especially in younger women. This may be true, but large-scale human studies offer no supporting evidence. Certainly, simple counts of "cancers" discovered by various screening modalities are insufficient without careful control of biases such as recent trends toward the inclusion of borderline or benign neoplasms, e.g., lobular carcinoma and intraductal carcinoma *in situ*.

There are three major reasons why data from the NCI-ACS BCDDP cannot be used to estimate the results of screening an average group of asymptomatic women. First, there is no control group. The screenees are likely to be atypical in many ways because women decide for themselves whether or not they will seek screening.

---

* Personal communication

Second, and perhaps more important, the results of the NCI-ACS program available to me do not distinguish between symptomatic and asymptomatic women.[1] The medical histories have been collected but not processed. Simple counts of breast cancers discovered may thus be seriously biased. If just two women in every thousand ask for screening because they have symptoms of breast cancer, they would account for over half of the cancers discovered to date. The screening of symptomatic women has not been seriously questioned, and mixing such a group with asymptomatic women simply and plainly destroys the value of the data for testing whether asymptomatic women (as defined here) should be screened. It should also be noted that even the unprocessed data on symptoms may not completely resolve this matter because of the likelihood that one or two women per thousand may falsely deny—to themselves as well as to the examiner—that they have any symptoms.

Third, that program was not set up to provide data of research quality, and the data are severely deficient or inaccurate in important ways. The most serious problems are that reporting of the number of "interval" cancers (those not found by the screening program) is at present seriously incomplete, and for those that were abnormal on screening by more than one modality, the recorded data are unreliable as to which modality or modalities should be credited.[40] Bross[11] and Fink[22] have discussed some of the definitions and problems in using data from that program for research purposes.

Cancer epidemiologists recognize that the number of cancers discovered in a screening program does not provide a direct index of benefits. Reasons include:

(1) For some forms of cancer, many or most patients already survive without the benefit of screening programs. While every additional life saved may be very much worth saving, it is misleading to attribute all survivals to earlier detection. For breast cancer, approximately 60% of patients now survive their disease.

(2) Some patients will die of their cancer despite earlier detection. Of 132 breast cancers found by the HIP screening program, at least 17 have already resulted in the death of the patient, including three cancers found only by mammography.[46]

(3) Self-selection may have a major impact. Health-conscious women (who might for that reason alone have earlier detection and above-average prognosis) may be especially likely to request screening; voluntary screenees may include a high proportion of women with above-average risks of developing breast cancer; and a small number of women who already have signs or symptoms of breast cancer may, for that reason, request (or accept) screening and distort the cancer discovery rate.

(4) While very nearly all of the general, or average, female population is free of symptoms of breast cancer, the small proportion with symptoms is extremely important. Thus even a random sample of the general population may yield screening results markedly at variance for those from a truly asymptomatic population. Cancer incidence rates among women who decline to participate in well-advertised and easily available screening programs may approach incidence rates among asymptomatic women in general; such rates are known to be lower than for women who do accept screening.[47]

(5) There is often a failure to distinguish between results of an initial round of screening examinations and results obtained over a regular series of follow-up examinations.

(6) Various biases are known to affect the survival rates of patients with cancers found by screening. The most important are the lead time bias and the length bias; these have been discussed elsewhere.[4,21,44] For example, Kusama *et al.*[27] and Spratt *et al.*[53] have discussed the relation between tumor volume doubling times and the probability of recurrence (no relation demonstrated) and between doubling times and survival (strong relation). These data as well as those of the HIP study[4] thus show a significant length bias effect. The effect of the length bias is pervasive and likely to be profound in breast cancer screening.

In summary, breast cancer screening can save lives, at least in the short run, but the contribution of x-ray mammography to that initial benefit is not clear. Estimates[4] are that mammography reduced the total breast cancer mortality in the HIP study group by not more than 10%, and possibly by much less. Shapiro[45] estimated that the exclusion of mammography from screening programs would reduce benefits by about one-third, implying a total mortality difference of about 10% under the conditions of the HIP study. Breslow *et al.*[10] have recently reviewed the data and concluded that "x-ray mammography led to an approximately 10–15% reduction in breast cancer mortality" but that there is reason to believe that the reduction would have been greater if participation by the study group had been more complete. The evidence indicates that annual mammography would probably not reduce total breast cancer mortality by as much as 20% below that attainable by annual history and physical examination, even if participation were universal. This estimate includes consideration of the value of other screening modalities, the frequency of cancers found between screening examinations, the deaths of some patients despite very early detection, and the pervasive effects of biases in the types of cancer found by screening.

Several important areas remain almost unexplored. One is the optimum frequency of screening for women who should have it at all, another is the hazard really presented by certain benign or borderline lesions detectable by mammography (lobular carcinoma *in situ*; intraductal lesions), and a third is the relationship among image quality, cancer detection rates, and radiation exposure with some of the newer ultra-low-dose techniques. The most important, however, may be the relation between the natural incidence of cancer and the risk of radiation exposure. Animal strains with a low incidence of some form of cancer are often resistant to the effects of carcinogenic agents, while strains with a higher "natural" incidence have a greater susceptibility to the induction of yet more cancers. Thus, are women already at high risk of breast cancer also at especially high risk for the induction of radiogenic cancers? If so, high-risk women may be the least suitable candidates for x-ray mammography. This possibility needs prompt and thorough evaluation.

Differentiation of Risks of Breast Cancer

Many factors are known to be related to the risk of breast cancer. A few that are associated with incidence rates below average are: 1) no family history of breast cancer, 2) two or more pregnancies, 3) first pregnancy before age 25, and 4) menopause before age 50. Is the presence of one or more indicators of low risk a specific contra-indication to x-ray mammography? No more than the absence of one or more such factors is a specific indication that mammography should be done. For example, about 90% of women with a history of breast cancer in a mother or sister do not themselves develop the disease.

If we had appropriate information, the risk of breast cancer for any given woman could be placed on a continuous scale from very low to very high. Thus we could identify 5% of women in whom the risk is highest, or 20% in whom it is highest, or even 95%. Recent statements to the press[16] implying that 80% of women are at higher risk than the other 20% are not very informative. Such statements would be true for any proportion between 0% and 100%. Further, such statements certainly do not imply that 80% of women have such a high risk of breast cancer that they should have annual mammographic screening, regardless of age. The 80% with highest risk may include 30% or more in whom the risk is still well below average. Certainly, it is misleading to imply that 80% of all women are at high risk of breast cancer when only 7% are ever found to have it.

With three exceptions, all of the risk factors now known for breast cancer have relatively low risk ratios (appoximately 3.0:1 or less). The exceptions are 1) age, 2) race, and 3) history of breast cancer on the contralateral side. Risk ratios of 3.0:1 are likely to be of marginal value in identifying the best candidates for mammography, unless several risk factors are present simultaneously and have independent or synergistic effects. One must also consider the entire medical history, not just present findings. Thus breast pain may sometimes be an indication for screening, but a long history of premenstrual breast pain (in the absence of other factors) is not, nor is a long and stable history of chronic cystic mastitis. The latter may even be a specific contraindication under some circumstances, because extensive fibrocystic changes can obscure signs of cancer on mammography. Recommendations for the screening of breasts that are large and difficult to examine by palpation seem particularly unwise. Not only does the preceding analysis of benefits still hold; the radiation risks may be significantly greater than for smaller breasts. This is because a greater volume of tissue is exposed and, perhaps more important, the higher entrance doses required for thick breasts result in a higher average dose in the expored tissues.

Davies and co-workers[17] recently took a large first step toward the differentiation of risks of breast cancer in the general population. They made two major simplifying assumptions that need to be verified: that the risk factors they selected for their analysis occur independently, and that the risks these factors generate are also independent on a multiplicative scale. Using these assumptions and risk estimates for individual factors already available from the literature, they obtained a nearly continuous spectrum of risks within each five-year age group from 40 to 65. If this work can be confirmed and clinically applied we might find, for example, that the risk of breast cancer is high enough to justify mammography for a very small but identifiable percentage of women aged 40–44 or for a much larger percent of women aged 55–59, with individual risks in each age group determined by the presence or absence of specific combinations of risk factors affecting that age group.

For each potential screenee, a separate decision must still be made which is based, in part, on the best possible overall assessment of the probability that she has a breast cancer involving each of three characteristics: It should be 1) presently unknown, 2) not discoverable by medical history and physical examination, but 3) discoverable by x-ray mammography.

Synthesis

Some elements of rational decisions on screening of individuals have been discussed. Rational decisions on the optimum use of x-ray mammography in whole screening programs clearly involve the same plus other factors. Some of the most important are: 1) the distribution of risk factors for breast cancer, including age, in the population to be screened; 2) radiation ~~doses~~ actually delivered to breast tissue; 3) the likelihood that the mammography system used at a given clinic will detect a breast cancer that could not be found by less hazardous means; and 4) the likelihood that a women with a cancer found early will survive, and that she would otherwise have died of the cancer. Lifetime patterns of screening must also be considered; for example, the woman who is screened annually from age 35 to 50 and then quits may have a greater likelihood of death from breast cancer than the one who starts at 35 and continues indefinitely, who in turn has a greater likelihood than the woman who does not start until she is 50 or older.

We now have most of the tools needed for the framework of a rational breast cancer screening program. McKeown[54] recently summarized some of the important principles for development of rational screening policies.

With respect to benefits, I estimate from the HIP data on rescreening that not more than 20% of all new breast cancers could be found by annual mammographic screening before they could be found in any other way. This figure is probably lower at young ages and higher at older ages, but I have not included an age adjustment here. I also estimate, after consideration of the length bias and other important factors, that the survival rate for these cancers would then be raised from 75% without screening to 95% with screening. Since we are dealing with causes of death, the question of "cure," as distinct from survival, does not arise.

The risks of ionizing radiation to the breast have recently been studied in detail by Upton *et al.*[55] They accepted that the dose-response relationship (tissue dose in rads) can be treated as linear regardless of dose and age at irradiation, and recommended that "the risk be assumed to approximate six cases of breast cancer per million women of ages 35 or older at risk per year per rad to both breasts, from the sixth year after irradiation throughout the remainder of life." This risk estimate can be used with standard life tables for U.S. females to determine the lifetime risk of various amounts of radiation at different ages. While this estimate has been criticized because it *is* an estimate, no alternative estimate has been proposed, developed, and defended with equal care (see, e.g.,[9]).

Under these conditions, but assuming a latent period of 10 years rather than five, an average tissue does of 2 rads would result in about 370 breast cancers for each round of screening of an average million American women aged 35–39 years; these cancers would then cause about 148 deaths. These figures and similar estimates for other age groups are given in Table 1. This table indicates that for screening a random sample of the population the frequency of short-term reduction in breast cancer mortality would just balance extra radiation-related mortality in the future for women aged about 55. This figure is dependent on the assumed 2-rad tissue dose; for a tissue does of 3 rads, risks balance benefits at about age 60; while for a 1-rad dose (now with the use of the lower efficacy of mammography in young women), they balance at about age 50.

These ages at which risks just balance benefits do not imply that screening is desirable for every woman who passes that age. First, we have already noted that women of identical ages may have widely differing probabilities of developing breast cancer. Second, I would not care to judge how many 55-year-old women would want to invest the time, effort, and money for a program

TABLE 1 Estimated Risks and Benefits from a Lifetime Screening Program for Unselected Women, by Age

Age at exam	New cancers per year (no radiation)[*]	Detectable only by mammography (annual screening)[†]	Lifetime risk of additional cancers, per exam	Estimated breast cancer deaths prevented[‡]	Estimated breast cancer deaths added[§]
35-39	533	107	370	21	148
40-44	1028	206	310	41	124
45-49	1560	312	260	62	104
50-54	1684	337	210	67	84
55-59	1883	377	160	75	64
60-64	2215	443	120	89	48

NOTE Values are per million women in the specified age group subjected to annual screening over their remaining lifetime at mean tissue dose of 2 rads per examination Figures are critically dependent on underlying assumptions, see text

[*] Source Third National Cancer Survey [10]

[†] Assume 20%

[‡] Assume survival raised from 75% to 95%, including adjustments for histologic types and length bias

[§] Assume 40% mortality

in which health benefits might just equal health risks.

While the model described here is sufficiently accurate for many purposes, it has several limitations First, it refers to screening of a random sample of the general population To the extent that we can identify women with risks lower (or higher) than average, the benefit curve moves downward (or upward) and the age to begin screening rises (or falls). For example, the analysis in the table has been redone on the assumption that 20% of all women can be identified as having zero risk, so that only 80% need screening at all. The point at which benefits begin to exceed risks with a 2-rad tissue dose is reduced by less than two years, from age 55 to perhaps 53 or 53½.

I must emphasize that this analytic model is generous in assuming that screening can reduce mortality from breast cancer in women of all ages; the only data on this point showed no reduction whatever in breast cancer mortality under the age of 50.

A statement by Dr. Arthur Upton[14] that a single mammographic examination might raise the lifetime incidence of breast cancer by not more than (and perhaps significantly less than) 1%, from 7 to 7.07/100 women, has been widely quoted. In less microscopic terms, a set of 15 mammograms would raise the lifetime incidence by not more than 15%. Would those same 15 mammograms, given annually over the 15 years from age 35 to 50, reduce short-term mortality by a comparable amount? It is most unlikely; only 30% of all breast cancers occur before age 50, most of the 30% are not detectable on annual screening, and well over half that can be detected are found by (sometimes only by) medical history or physical examination.

Guidelines

Breast cancer screening can offer important short-term improvements in the survival of those few women found to have cancer, and mammography can contribute to those improvements. Yet we must consider the costs, especially in terms of future illness and death from radiogenic cancer. Individual decisions must still be made for individual patients, largely on the basis of 1) known risk factors for breast cancer, and 2) radiation doses actually delivered in each center, hospital, clinic, or office. Such doses may be difficult for the referring physician to determine. However, the following guidelines would help to avoid doing more damage than good:

(1) Women should be told that periodic screening may prevent as many as one in three deaths from breast cancer, but that mammography accounts for only a part of that improvement while it presents a significant long-term danger. Expectations that mammography will reduce short-term mortality by more than 20% below that attainable by other modalities are unrealistic and should be actively discouraged

(2) Any woman over age 35 may benefit from annual screening by medical history and physical examination, and no risk is involved. These should always be done before any decision on whether mammography is also indicated.

(3) No physician should allow his patients to be screened by mammography unless the equipment has been recently tested and adjusted, all steps in the examination are per-

> formed by professional staff specifically trained for those steps, and the average tissue dose for a complete set of films has been measured with the specific piece of equipment and specific techniques to be used and is known to be less than 1 rad
>
> (4) If the average tissue dose is less than 1 rad per complete examination, and if the screenee has no signs, symptoms, or history that would require biopsy if mammography were not available, mammography may offer some benefit. I would use it as follows for various age groups, though the age ranges are subject to change as we learn more about the effect of combinations of natural risk factors and, especially, whether natural factors are synergistic with radiation risks Under 50: Mammography is appropriate only for a very small percentage of women known to be at extremely high risk; average or even moderately increased risks do not overcome the future hazards. Ages 50 to 60: Mammography seems beneficial for more women as they move from age 50 to 60; the break-even point depends on identifiable risk factors. Over 60. Mammography seems to offer some net benefit for most women over 60, excluding only those thought to have unusually low risks of breast cancer.
>
> (5) For women below age 35 or those with symptoms of breast cancer at any age, mammography should be the last step before a decision on the need for surgical biopsy, and should be done then if, and only if, the mammographic findings will conclusively determine how or whether biopsy is to be performed. When indications are sufficient for a biopsy despite negative x-ray findings, the x-ray results may be irrelevant and the patient should be spared unnecessary exposure (and expense), though mammography of just the opposite breast may still be indicated.

Peck and Lowman[36] have suggested somewhat less restrictive guidelines on mammography. Those of the American Cancer Society[3] appear far too generous in view of the risks and limitations of the procedure, as do those expressed in a recent editorial in *CA*[25] and those of the American College of Radiology (see, e.g., attachment to reference 44).

Prospects

Scientific disagreements over risks and benefits in breast cancer screening first came to public attention only 18 months ago, but there have already been important changes. The consent form used in the BCDDP has been revised and now mentions the possibility of radiation damage. That statement is still very weak, and further revisions are under consideration. A second change is that the ACS and the NCI have explicitly withdrawn support from indiscriminate population-wide screening of women under age 50.[23] Third, it has become clear that efforts directed toward the reduction of radiation doses can be successful. Thus average tissue doses in the BCDDP have been sharply reduced and now seem to be a little over one rad, as estimated from reported air doses.[61] Finally, and most important, the change in attitudes has been marked. Both health professionals and the public have become more sensitive to questions of risks and benefits. The next step should be the development of specific guidelines on radiation dose levels, with a requirement that screenees be informed of the guidelines as well as the doses actually used.

Where should we go from here? I see several hopeful signs for the future. Increasing dissatisfaction with the present practice of mammography has helped to accelerate research and development of new reduced-dose techniques. Some should lead to substantial improvements in present methods, and some to entirely new radiation sources, image receptors, or methods of interpretation

Two other methods for the detection and localization of abnormal breast masses have received much attention. Thermography has now been applied on a broad scale, but acceptable rates of false positive and false negative reports have been attained only in a few centers with special interests and competence in this technique. This situation could change with further research or perhaps with further education of staff, but thermography may never become a major tool in the screening of asymptomatic populations.[20] Ultrasound techniques also show promise, but applications are still well in the future. Dodd has discussed these matters elsewhere in this symposium.

Research on biochemical and other markers of breast cancer has also been expanded. While such techniques might not in themselves localize tumor masses, positive findings could help to identify a small subgroup of screenees who warrant much more intensive efforts at cancer detection, possibly including mammography

Finally, there are still some serious gaps in our basic knowledge about breast cancer screening. Examples are the incomplete understanding of the optimum frequency for screening, the relation between image quality and dose, and the true nature of some of the lesions found by mammography. Further attempts should also be made to correlate the risk of future breast cancer with the background appearance of the breast tissue (parenchyma) on a single set of mammography films,[40] though one attempt to confirm this work[41] was not successful

The controversy over risks and benefits in breast cancer screening, and especially over x-ray mammography, has been traumatic to some of the public as well as to those whose professional work is related to screening. However, the public has a right to full information on both sides of the matter

My own assessment is that properly designed, properly targeted breast cancer screening programs can significantly contribute to the public health even with today's techniques, but that indiscriminate and uncontrolled programs for annual screening are dangerous

REFERENCES

1 Acton B Personal communication

2 American Cancer Society New York City Division Professional Education Department Urgent Message Mammography Benefits versus risks 1 page, 1976

3 American College of Radiology Update on mammography *ACR Bull* 32 1 3 1976

4 Bailar J C Mammography A contrary view *Ann Intern Med* 84 77-84, 1976

5 Bicehouse H J Survey of mammographic exposure levels and techniques used in Eastern Pennsylvania *In* Proceedings 7th Annual Conference of Radiation Control Program Directors Washington, D C, U S Govt Print Off, Publication EDA 76-8026 1976, pp 136-143

6 Bicehouse H J Personal communication

7 Boice J D and Monson R R Breast cancer following repeated fluoroscopic examination of the chest To be published *J Natl Cancer Inst*

8 Bond V P Cronkite E P, Lippincott, S W *et al* Studies on radiation-induced mammary gland neoplasia in the rat III Relation of the neoplastic response to dose of total-body radiation *Radiat Res* 12 276-285, 1960

9 Breast Cancer Detection and Mammography Transcript of meeting, 19 July 1976 National Cancer Institute Bethesda Md

10 Breslow L Progress Report submitted to Dr Guy R Newell National Cancer Institute, Bethesda, Md, 15 July 1976 Revised version to be published *J Natl Cancer Inst*

11 Bross I D J Letter to Dr Diane Fink, 26 November 1976

12 Brown J M Linearity vs non-linearity of dose response for radiation carcinogenesis *Health Phys* 31 231-245, 1976

13 Chang C H J, Sibala, J L, Martin, N L *et al* Film mammography New low radiation technology *Radiology* 121 215-217, 1976

14 Chiacchierini R P, Lundin, F E, and Scheidt P C A risk/benefit analysis by life table modeling of an annual breast cancer screening program which includes x-ray mammography *In* Proceedings, Third International Symposium on the Detection and Prevention of Cancer New York N Y 26 April-1 May, 1976 In press

15 Cukier D S, Lopez, F A, and Maravilla, R B, Jr Efficacy of a one-view follow-up mammogram in screening for breast cancer *JAMA* 237 661-662 1977

16 Cutler S J and Young J L, Eds Third National Cancer Survey Incidence data *Natl Cancer Inst Monogr* 41 110-111 1975

17 Davies D F, Torng, A Morris, E B *et al* Quantification of prognostic characteristics of breast cancer Submitted for publication 1977

18 Eddy D M A methodology for evaluating breast cancer screening programs Personal communication

19 Ellett W H M, and Richardson, A C B Estimates of the cancer risk due to nuclear-electric power generation Washington, D C, Environmental Protection Agency Technical Note ORP/CSD-76-2, 1976

20 *FDA Drug Bulletin* Thermography restriction 6 32, 1976

21 Feinleib, M, and Zelen, M Some pitfalls in the evaluation of screening programs *Arch Environ Health* 19 412-415, 1969

22 Fink, D J Letter to Dr Irwin D J Bross, 18 November 1976

23 Fink, D J, and Holleb, A Letter to Project Directors, Breast Cancer Detection Demonstration Program, 23 August 1976

24 Holleb, A Quoted in *Washington Star*, 8 November 1976

25 Holleb, A I Restoring confidence in mammography Editorial *CA* 26 376-378, 1976

26 Jans R G The options Mammography quality assurance program *In* Proceedings, Eighth Annual Conference on Radiation Control Springfield, Ill, May 1976 In press

27 Kusama, S, Spratt, J S, Donegan, W L *et al* The gross rates of growth of human mammary carcinoma *Cancer* 30 594-599, 1972

28 Li, F P, Cassady, J R, and Jaffe, N Risk of second tumors in survivors of childhood cancer *Cancer* 35 1230-1235, 1975

29 Libshitz, H I, Fetouh, S, Isley, J *et al* One-view mammographic screening? *Radiology* 120 719-722, 1976

30 Lundgren, B, and Jakobsson, S Single view mammography A simple and efficient approach to breast cancer screening *Cancer* 38 1124 1129, 1976

31 Malone, W F Radiation exposures and dose reduction in BCDDP Unpublished report, July 1976

32 Malone, W F Personal Communication

33 McGregor, D H, Land C E, Choi, K *et al* Risk of breast cancer in Japanese A-bomb survivors To be published, *J Natl Cancer Inst*

34 McKeown, T An approach to screening polices *J R Coll Physicians Lond* 10 145-152, 1976

35 Morgan, K Z Reducing medical exposure to ionizing radiation *J Am Ind Hyg Assoc* 36 358-368, 1975

36 Moskowitz, M, Pemmaraju, S, Fidler, J A *et al* On the diagnosis of minimal breast cancer in a screenee population *Cancer* 37 2543-2552, 1976

37 National Council on Radiation Protection and Measurements Review of the Current State of Radiation Protection Philosophy Washington, D C, NCRP Report No 43, 1975

38 Peck, D R, and Lowman, R M Mammography Current application *JAMA* 236 1886-1890, 1976

39 Pochin, E E Radiology now Malignancies following low radiation exposures in man *Br J Radiol* 49 577-579 1976

40 Pomerance, W Letter to Dr Marvin Zelen, 18 November 1975

41 Rideout, D F, and Poon, P Y Relationship of mammographic appearance to high risk of breast carcinoma Presented at Second Annual Mid-American Breast Cancer Symposium, Madison, Wis, 6 November 1976

42 Rossi, H H, and Kellerer, A M Radiation carcinogenesis at low doses *Science* 175 200-202, 1972

43 Russell, C Washington Star, 10 November 1976

44 Ryan, A J Is mammography for breast cancer a factor in increasing survival? *Postgrad Med* 60 61-63, 1976

45 Shapiro, S Evidence on screening for breast cancer from a randomized trial *Cancer* 39 2772-2782, 1977

46 Shapiro, S Personal communication

47 Shapiro, S, Strax, P, Venet, L *et al* Changes in 5-year breast cancer mortality in a breast cancer screening program *In* Proceedings, Seventh National Cancer Conference Philadelphia, J B Lippincott Co, 1973, pp 663-678

48 Shellabarger, C J Radiation carcinogenesis Laboratory studies *Cancer* 37 1090-1096, 1976

49 Shellabarger, C J, Brown, R D, Rao, A R *et al* Rat mammary carcinogenesis following neutron or x-radiation *In* Biological Effects of Neutron irradiation, International Atomic Energy Agency, Vienna, 1974, pp 391-400

50 Shore, R E, Hempelmann, L H, Kowaluk, E *et al* Breast neoplasms in women treated with x-rays for acute postpartum mastitis To be published, *J Natl Cancer Inst*

51 Shwartz, M Analysis of the benefits of serial screening to detect early breast cancer Detroit, Michigan Cancer Foundation, 1976

52 Simon, N Cancer of the breast induced by radiation, with comments on mammography and treatment of acne *JAMA* 237 789-790, 1977

53 Spratt, J S, Kaltenbach, M L, and Spratt, J A Cytokinetic definition of acute and chronic breast cancer *Cancer Res* 37 226-230, 1977

54 Upton, A C Letter to Dr Frank J Rauscher, Jr, 20 July 1976

55 Upton, A C, Beebe, G W, Brown, J M *et al* Draft report, NCI Ad Hoc Working Group on the Risks Associated with Mammography in Mass Screening for the Detection of Breast Cancer, November 1976 Revised version to be published, *J Natl Cancer Inst*

56 Urbach, F. Personal communication

57 Vogel, H H, and Zaldivar, R Neutron-induced mammary neoplasms in the rat *Cancer Res* 32 933-938, 1972

58 Walburg, H E, Jr Experimental radiation carcinogenesis *In* Advances in Radiation Biology New York, Academic Press, 1974, pp 209-253

59 Wochos, J F, and Cameron, J R Patient exposure from diagnostic x-rays An analysis of two years of NEXT data Bureau of Radiologic Health, Food and Drug Administration In press

60 Wolfe, J N Breast patterns as an index of risk for developing breast cancer *Am J Roentgenol Radium Ther Nucl Med* 126 1130-1139, 1976

61 Wolfe, S M Letter to Dr. Theodore Cooper, and attached report by S M Wolfe and R Warner, 9 November 1976

62 Wootton, P Interim report Mammographic exposures at the Breast Cancer Detection Demonstration Project screening centers *Am J Roentgenol Radium Ther Nucl Med* 127 531-533, 1976

63 Wright, D J, Nichini, F M, and Stauffer, H M Letter to the editor *Br J Radiol* 44 480, 1971

64 Zelen, M Theory of early detection of breast cancer in the general population *In* Breast Cancer Trends in Research and Treatment J C Heuson, W H Mattheiem, and M Rozencweig, Eds New York, Raven Press, 1976; pp 287-300

University of New York at Buffalo

IN ZELEN, Director
AL LABORATORY

FACULTY OF NATURAL SCIENCES AND MATHEMATICS

Attachment 5

July 16, 1973

Dr. Frank J. Rauscher, Director
National Cancer Institute
National Institutes of Health
Bethesda, Maryland 20014

Dear Frank:

This letter is to strongly protest the present plans for the National Breast Cancer Demonstration Project. The Project is ill-conceived and is not likely to result in significant patient benefit. Earlier, I had written John Bailar on this matter, but he indicated his authority is limited in this Project. Enclosed are comments on the National Breast Cancer Demonstration Project and on the HIP Breast Screening Study which I had earlier circulated to Dr. Bailar. I wish to urge that a meeting be set up as soon as possible to allow the chief backers of this project to publicly defend their point of view.

With kind regards,

Sincerely,

Marvin

Marvin Zelen
Professor of Statistics

MZ:gp

c.c. J. Bailar

Tab 21-2c
Zelen #1

Comments on the National Breast Cancer Demonstration Project

These comments were written after making three site visits at possible participating institutions.

1. The proposed protocol will not be able to generate data which will help answer questions about the benefit of early detection using mammography, themography, and a physical examination. It is by no means clear that detection mammography is beneficial in prolonging survival. This is contrary to the widely held view that the HIP Study has demonstrated this. (See my critique of the analysis of the HIP Study).

2. The most serious drawback to the protocol is the lack of a control group. Although it was continually pointed out in the site visit that this is not a "Study", nevertheless the plan is to do follow-up on all people for five years. Also the pathology form is certainly not a routine pathology form. There would be no need for any follow-up on the extensive path form unless someone is trying to learn "something".

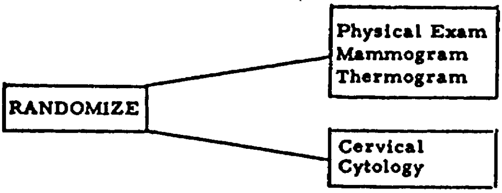
3. The age group chosen for the study is set much too low (35) to yield many new cases. The incidence of the 35-44 age group is about 2 per 5,000 which probably means a prevalence rate of 4-6 per 5,000. Since there does not seem to be any well defined population, and women are to be contacted through employment unions, places of work, etc., there is a very good possibility that a significant number of women appearing for the examination will be of working age and in the under 50 age group. As a result the yield of new cases may be quite low.

4. In view of the above difficulties, it would be wise to re-consider the entire protocol. If the only object is to set up mammography and thermography units to detect brest cancer early, why not simply give $100,000 to any institution who wishes to participate with the proviso that these institutions screen some minimum number per year free of charge.

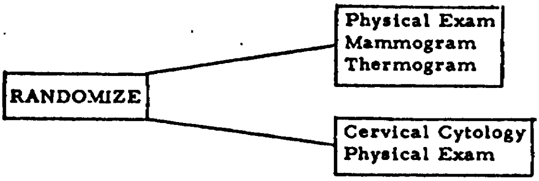
5. On the other hand, this program not only presents a unique opportunity to learn something about the early detection of brest cancer, but cervical cancer as well. This may represent a unique opportunity to prospectively assess the benefits of cervical cytology. I wish to suggest that the protocol for detecting brest cancer be modified so that a woman volunteer will be randomized to either a brest examination or a cervical smear sample taken. Thus there will be two randomized groups - a screened group for brest cancer and one for cervical cancer. Each serves as the control group for the other.

An alternate possible plan is to have the cervical cytology group also receive a physical examination. Thus with regard to brest cancer, one would have two groups. A group having a physical examination only and one having a mammogram and thermogram in addition to the physical examination. Below is a diagram of each plan.

Plan I



Plan II



If Plan I is adopted, one would be able to evaluate the benefits of the screening programs by comparing the:

(i) death rates due to brest cancer

(ii) death rates due to cervical cancer

Comparison of the death rates between the two groups in Plan II would enable one to obtain the same information as Plan I for cervical cancer. However with regard to brest cancer one would be able to directly assess the benefits of a Physical Exam alone versus a Physical Exam combined with mammography and thermography.

M. Zelen, March 1973

Ellen # 2

Comments on the HIP Breast Screening Study

1. These comments are based on information published in the JAMA 1971 article. Some of these comments may have been answered by subsequent unpublished papers which I am unaware of.

2. The HIP study represents one of the most carefully designed and executed studies of early detection ever done. Nevertheless questions do arise with regard to interpreting the reported HIP results. The interpretation is complicated because of two facets of early detection case findings which are not well understood by many clinicians and are discussed below. These are (i) Length biased case finding, and (ii) Lead time biasing.

(i) Length biased case finding. The phenomena of early detection case findings tends to detect cases which have longer pre-clinical durations. (Longer pre-clinical duration is associated with slow growing pre-clinical disease).

This idea is demonstrated in figure 1. The varying lengths of the horizontal lines reflect the fact that there is a probability distribution for the duration of pre-clinical disease. The entire early detection process is equivalent to placing a vertical line at random (corresponding to the screening point) on the figure. The intersection of the vertical line with a horizontal line corresponds to a case found by screening. Note that the vertical line is more likely to intersect a longer horizontal line (longer pre-clinical duration) than a shorter horizontal line (shorter pre-clinical duration). Thus any screening program does not find cases at random. Screening programs tend to find people with longer pre-clinical duration. Hence, if the clinical course of the disease is correlated with the pre-clinical course, individuals diagnosed in a screening program will be observed to survive longer (from point of diagnosis) even though treatment may not be enhanced by earlier case detection. This is the reason one must deal with the mortality of the entire population group. The HIP investigators are aware of this bias and for that reason present most of their evidence in terms of total mortality rates for the study and screened groups.

(ii) Lead time biasing. Survival comparisons between cases found by screening and those in the control group are made difficult because the cases found by screening have a different origin (starting point) than those in the control group. Figure 2 illustrates these ideas for a hypothetical case where it is assumed that early case finding does not result in cure or increase in survival. In this figure we have:

AD = Interval denoting total time with disease from inception to death;

BD = Interval denoting survival if patient is diagnosed by screen at point B;

CD = Interval denoting survival if patient is diagnosed under routine medical care and is clinically diagnosed at point C.

It is clear from the diagram that although the patient dies at point D, the apparent survival from point of diagnosis and treatment will always be larger if the disease is found by an early detection program. Hence, a direct comparison of the survival of those found only by a screening program will always be invalid.

However, such a comparison can be made valid by adjusting the survival of the screened cases by the interval BC. This interval BC corresponds to how much earlier the disease is detected by the screening program relative to not having a screening program. This is what the HIP papers refer to as the lead time. Of course, one cannot directly observe the lead time for any patient. The best that can be done is to estimate the mean lead time from the data. Furthermore, the mean lead time is different for cases found at the initial screen and those found in subsequent periodic screenings.

BEST COPY AVAILABLE

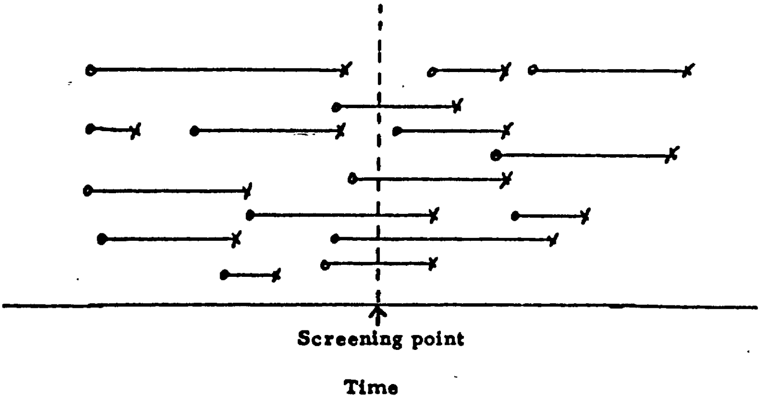


Figure 1. Duration of pre-clinical disease for a population. Each horizontal line represents a case having the disease. Length of horizontal line represents duration of pre-clinical disease. Left point of line (indicated by o) refers to beginning of disease; right hand point (indicated by x) refers to time when disease is clinically diagnosed under routine medical care. Dotted vertical line at screening point intersects cases found by early detection examination.

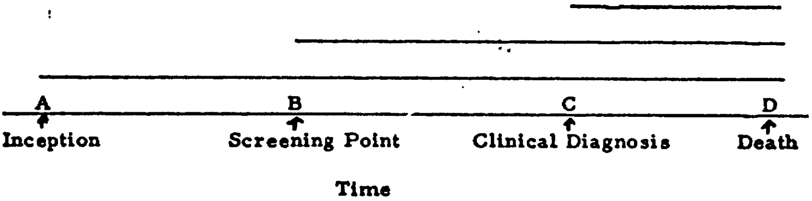


Figure 2. Relationship between time from treatment to death under various types of diagnosis.

3. Evidence of Axillary Nodal Involvement. The HIP Study shows that the proportion of cases with no evidence of axillary involvement is high (70%). Since a screening program always tends to find cases which have slower growing disease (longer pre-clinical durations), the relatively high proportion of lack of nodal involvement is exactly what one would expect to find in any screening program. This figure is simply a confirmation that slow growing disease tends to have fewer patients with nodal involvement. It should not be interpreted as scientific evidence showing that the early detection system is beneficial.

4. Relative Benefit of Mammography versus Physical Exam. Cases in the Study Group initially diagnosed by the screening program could have been diagnosed by (i) mammography alone, (ii) physical exam alone, or (iii) both modes of diagnosis. Nowhere have the HIP investigators published results showing the reduction in mortality rate attributed to each mode of diagnosis. It might very well be that the benefits from early detection only accrue to those cases which could only be diagnosed by mammography or perhaps those diagnosed by a physical examination are the ones principally benefiting.

From the HIP Study we can calculate that 85 confirmed cancers (from a total of 127) would have been diagnosed if mammography had not been a mode of diagnosis. Thus 2/3 of the confirmed cancers would have been diagnosed simply by a physical exam. However, we do not know the benefits of this group with regard to reduction in mortality. If one is using the HIP Study as the main source of scientific information for planning the National Demonstration Project, then it is absolutely essential to separate out the relative benefits of the physical exam from other modes of detection. It should be possible to do an analytic study to show whether larger numbers of case findings would result from (say) 100 centers doing physical exams only compared to 20 centers conducting physical exams combined with other modes of detection.

5. Analysis of Mortality. The analysis of the mortality figures has not been carried out in strict accordance with the experimental plan. The original plan selected 31,000 pairs of women, stratified by age, size of insured family, and the employment group. This means that all analyses should have been carried out on the basis of the initial pairing. If any member of the pair dropped out (death, diagnosis of breast cancer, etc.) prior to the initial screening exam, that pair should be eliminated. The mortality comparisons are then to be made within a pair. That is, the status of each member of a pair would be: alive (no breast cancer), alive (breast cancer), dead (cause other than breast cancer), dead (breast cancer). The only pairs which are involved in the analysis of mortality are those in which at least one member has died. If the screening is beneficial, then one would expect that the difference in survival of a pair (where at least one member has breast cancer) would indicate larger average survival for the study group. (It is too complicated to outline full details of analysis in this critique). However the general idea of making comparisons within a pair would be a much more sensitive way of analyzing the mortality data. The analysis of mortality in the 1971 JAMA paper is not a sensitive method of analysis as it ignores the initial pairing of the women.

6. Analysis of case fatality rates. The analysis of the case fatality rates depends critically on the estimate of the average lead time used to adjust

the study group. The value used in the JAMA paper was one year. This value was taken from an earlier paper (Hutchinson and Shapiro JNCI (1968)). The average value of one year mean lead time is an under-estimate for the mean lead time of the first screen. My calculations indicate that the mean lead time is nearer to two years (cf. Biometrika 1971). Furthermore, the mean lead time for cases detected at the periodic screens is even larger. As a result, it is my opinion that all analysis dealing with the case fatality rates are incorrect.

SCHOOL OF MEDICINE
DEPARTMENT OF SOCIAL AND PREVENTIVE MEDICINE
BALTIMORE, MARYLAND 21201

FEB 6 1973

ATTACHMENT 6

January 31, 1973

Dr. Kenneth B. Olson, M.D.
Division of Cancer Biology
and Diagnosis
National Cancer Institute
Building 31 - Room 3A-C5
Bethesda, Maryland 20014

Dear Dr. Olson:

I enclose my few notes about the Breast Cancer Program. I hope they are of some use to you.

Sincerely yours,

Maureen Henderson, M.D.
Professor and Chairman
(Signed in Dr. Henderson's absence)

MH/dh
Enc.

BEST COPY AVAILABLE

Breast Cancer Demonstration Project

The document does not specify the overall objectives of the program which will support a specified number of centers. From discussion during the last meeting of the diagnostic research review group, I gained the impression that the major objectives was to demonstrate the mechanism for implementation of programs to screen a variety of different groups of women for high risk of breast cancer. Three methods will be used in parallel i.e. all patients will be subjected to all three screening tests irrespective of the results of each. It is assumed that an implementation of this series of demonstration programs will provide information about operational problems in a variety of populations and some information about the relative efficiency of each of the three screening tests alone and in tandem (i.e. If the individuals positive on one test are then subjected to the second and those positive on the second subjected to the third.)

The basic purpose of screening is to identify individuals who should be subjected to diagnostic procedures. A fundamental premise of all screening programs is that they are implemented within medical care delivery programs where diagnostic procedures are systematically available for individuals identified as positive screenees. As I read the introductory description of the projects to be supported in this program, it suggests that they will not conform to this basic

BEST COPY AVAILABLE

premise. The literature is full of evidence that screening programs outside systems of medical care are inefficient and should not be developed. I am surprised that this fundamental question was not reviewed at the outset of the proposed program. One fundamental requirement for support should be evidence that the individuals to be screened are in a system where diagnostic procedures and necessary therapy can be easily and automatically arranged.

There is no justification for the choice of 5,000 individuals as the base population to be screened. Is this the number that provides a good cost, effective and efficient program? What are the estimates of the numbers of diagnostic procedures, pathological studies, and surgical and radio-therapeutic management procedures that will be required to complement a screening program in a population of 5,000 women?

What criteria will be used to demonstrate the success of: (1) each project within the program and; (2) of the overall program? The criteria for success should be specified before the program is implemented so that appropriate measurements can be applied throughout the period of support.

The aspects of the study that deserve more attention will be described under the following headings:

(1) Recruitment
(2) Screening
(3) Follow-up procedures

Recruitment

The program is designed to provide free screening to low income groups of women. There is no description of any age limit for entry into the screening programs and the possibility of screening 5,000 or more young women with a very low risk of breast cancer is not mentioned. If there is an educational rather than case focus to this program, it is not specified. If education is a major component, it would be important to focus the program towards young women (even school girls) with virtually no likelihood of getting a yield of positive screenees that make each local project cost effective.

What yield of (a) positive screenees, (b) identified cases will be accepted as appropriate for a project?

Screening

I see no purpose at all in much of the information to be gathered to describe each patient. This project does not have the population base for epidemiologic studies. The use of each item for purposes of (a) patient care (b) program assessment should be justified before it is included.

Follow-up

The follow up of the types of populations described in the protocol is a horrendous business. Much more costly and intensive [illegible] of tracing and participant contact will be necessary.

BEST COPY AVAILABLE

ATTACHMENT 1

Comments on Breast Cancer Screening

William Taylor

I have just returned from visiting three institutions which are proposing to establish a demonstration project in breast cancer screening. The institutions are Georgetown University, Emory University School of Medicine, and St. Vincent's Medical Center, Jacksonville, Florida.

From none of the proposals and from no one on our Committee was I able to obtain a clear statement of the purposes of such a breast cancer screening undertaking. All implied that they wished to find cases of breast cancer "earlier." None of them, though, indicated, "earlier than what?" No one showed any particular concern about defining the women who were to be screened. Because of this I found it difficult to distinguish between a good screening program and a poor one. Therefore, I have tried to describe some purposes of a breast cancer screening project which might make such projects subject to evaluation by comparing actual performance against desirable performance.

Of course, it is understood that the ultimate objective is to reduce breast cancer mortality. This reduction is assumed to follow as a result of

(1) finding cases of breast cancer earlier than they are presently being found,

(2) seeing that adequate medical care is made available and

(3) persuading women having breast cancer to accept such care.

I think these three items constitute reasonable objectives of a breast cancer screening program. There are others having to do with completeness of coverage, efficiency of operation, test validity, etc.

Obviously, some sort of breast cancer screening goes on now. This occurs whenever a women first finds a lump in her breast and goes to see a doctor. The woman has in effect screened herself. In an extreme case, screening

BEST COPY AVAILABLE

occurs only when a woman, in an advanced stage of breast cancer, feels so much pain that she finally goes to see a doctor to find relief. The opposite extreme is the woman who goes as part of her routine health examination to receive a breast cancer screening test in the same sense that she gets a chest x-ray, urine analysis, and Pap smear. These examples concern women who have been to their doctors and then have been referred by them for mammography or other breast cancer screening. These are clearly the ones which the present system is reaching.

The problem I want to discuss now is the following: If a new screening program is installed and it only receives women who have already sought help or routine breast screening from a physician, nothing new has been done and nothing new should be expected. I would like to know for each woman coming in to a screening center why she came. Was it because she thought it was a generally good idea or because she felt a lump or because her physician had sent her? From data such as these, we could determine the number of new women attracted by the screening center and this would then give us a handle on whether the screening is effective or not.

Another purpose of screening might be said to be to screen at appropriate intervals all women in a given area beyond a certain age. For instance, all women over 45 should be screened at least once a year for breast cancer by mammography, thermography or xerography, and in all cases by the addition of a competent doctor's physical examination. If we make such a rigid requirement, it is obviously impossible for a demonstration screening center to accomplish this in any large community. One might, in the case of Washington, D.C. or Atlanta or Jacksonville, pick out some sub-area of the community, direct particular attention to that area, make use of the knowledge of the number of women over 45 from available census figures, and see how close to 100 percent the screening center comes in attracting women for one of the appropriate

BEST COPY AVAILABLE

screening procedures. A demonstration breast cancer screening center set up in a small to medium-sized town might well take on the entire town as a task for screening. In this case, evaluation of the completeness of the program should be possible.

We turn now to the other principal goals of the screening center--namely making sure that adequate medical care is available and persuading women to accept such care. Somehow, the screening center has got to set up a system whereby, whenever a woman is found with possible breast cancer, medical care is available for her. This may involve getting cooperation of a number of physicians who are willing to see such women and assigning women to these physicians in some sensible way. Of course when women already have their own doctor, the case is referred to that doctor. However, it is not always certain that women will take advantage of medical care. Therefore, the center has got to have some kind of a follow-up system particularly aimed at women who are suspected to have breast cancer so that the effectiveness of the screening can be determined in terms of the number of women who actually receive the care which is made available in cases where the screening has actually found someone. In none of the three sites that I visited recently, was any real, sensible effort made in terms of follow-up to see that women screened receive and accept the medical care that is considered appropriate. In addition, none of the institutions that I visited had really addressed themselves to the general problem of repeat screening for women who successfully passed one screen. This means that women must be screened again and again, and a system for finding these women, keeping track of them, and bringing them back must be devised. The success in bringing them back for repeated screening will possibly be quite low in some areas and yet the importance of the screening program may well rest on the ability to screen

BEST COPY AVAILABLE

frequently enough so that breast cancer can in fact be found early. The initial screening, of course, is detecting breast cancer which may have been underway for a long time. It is the new cases that are the ones we want to find, particularly the asymptomatic ones unsuspected by the woman herself. Therefore, I think an important part of the screening evaluation is the ability of the screening organization and the volunteer organization associated with it in getting women to come repeatedly.

Dr. William Taylor
Mayo Clinic
November 22, 1972

ATTACHMENT 8

UNIVERSITY OF WASHINGTON
SEATTLE, WASHINGTON 98105

School of Public Health and Community Medicine
Department of Epidemiology and International Health

June 30, 1973

John C. Bailar, III, M.D.
Deputy Division Director
Cancer Control Program
National Cancer Institute, NIH
Bethesda, Maryland 20014

Dear Doctor Bailar:

I have recently had the privilege of acting as a member of a site visit team under the chairmanship of Dr. Sam Taylor for the Breast Cancer Detection Demonstration Project, visiting the Jamaica and Wycoff Hospitals in New York, Johns Hopkins Hospital, and the University of Michigan. We have done our best to give the Advisory Group the information it needs to make decisions between the various institutions that are competing to join this project. However, in working with my colleagues at this task it has seemed to me that there are a number of points about the broader strategy of this project which should be raised. The simplest way to organize these comments is to follow the stated objectives of the project as given to us in Section I of your manual.

Objective #1 - "To find out if research methods for the detection of breast cancer can be applied to the general population through regular medical channels".

The numbers that each institution is asked to deal with--about 5,000 women a year--is perhaps 1 to 2 percent of the total population the institutions serves. This figure will be lower for the larger hospitals and somewhat larger for the smaller hospitals serving crowded urban areas. Nationally, if we are dealing with 25 institutions, this means 125,000 women a year. This again means a few percent of the total adult female population at risk. All adult women are at risk from breast cancer, and to control the disease with presently forseeable treatment we need to reach all of the cases early. It is quite certain that the sample acquired as volunteers, and comprising less than 5% of the total at risk, will be drastically unrepresentative of the total population. It will tell us virtually nothing about the problem of reaching the average woman, let alone the reluctant. Thus the project is certain to provide the target numbers of women--and the experience of the centers that have begun confirms this--but we shall not know about the effectiveness of the American Cancer Society's volnteer workers to act as the medium for a true program to seriously reduce the mortality and misery from breast cancer in the total American population through the medium of current methods of early detection and contemporary surgery. A strategy which would have been much more informative would have been to establish defined populations and see if the volunteers of the American Cancer Society could bring in 70 to 80 percent of women at risk. This is a requirement if we are to substantially reduce the toll of breast cancer without some major advance in treatment.

Some information will be provided by the present study design about the way in which women cope with the requests for biopsy and of the present medical arrangements to deal with the physical demands and consequent costs of the volume of surgery produced by these studies. But again American medicine is fairly flexible, and will probabl be able to cope with the biopsies (assume to be ten times the number of cancers) produced by these small samples scattered across the country. But this ability is of little help in extrapolating to the very large physical demand of a program that reaches most of the women at risk. In the very long run, an effective program of early diagnosis of breast cancer would (apart from its value to the individual citizens) produce some balancing reduction in work for surgeons and hospitals in terms of late major surgery and terminal care, and this should be set against the extra biopsies. The problem of the total surgical and medical load of different strategies could be studied again in small defined populations, and the argument will remain hypothetical until this is done. In sum, the first objectives of the project will easily be achieved. But this success will tell us very little about the real problems of extending current techniques for the early diagnosis of breast cancer to a substantial fraction of American women who are going to develop this disease in any year.

Objective #2 - "To determine if a negative thermogram is sufficient to preclude the use of clinical examination and mammography in the detection of breast cancer".

We know that the proportion of false negatives from thermography is fairly high. There is a whole range of unpublished studies and the state of the art is changing quite quickly. This Demonstration Project will provide some more figures which will no doubt fit into the rest of the literature. The addition of these do not help us with the moral and political questions as to whether a simple test with this degree of error is better for general use than the much more expensive and perhaps unfeasible on a large scale use of mammography. There is also the problem of radiation dosage on a population scale in mammography.

Objective #3 - "To determine if American Cancer Society volunteers can provide a population of women for screening with adequate follow-up phases of this study".

They can clearly provide the women and it will be interesting to see if they can operate the follow-up phases as well. In fact, from my conversations with the different hospitals, most of them seemed to be planning to operate the follow-up system through their ordinary internal arrangements, but no doubt this will be worked out. We shall still be looking at the few percent of women with highest interest in the early detection of cancer, and the problem will remain that these are probably much easier to follow up than the average woman or the reluctant woman.

Objective #4 - "To determine or confirm the observation that non-palpable breast cancer properly treated will provide more years free of known disease than waiting for palpable evidence of disease".

This is not a very happily written section, but I think that we can assume proper correction for the mere gain in time while the disease is developing to the palpable stage. The problem here is, of course, the absence of a control group. This is particularly difficult for two reasons. We are not searching for a large effect; with the common techniques of today, where essentially the woman finds the tumor for herself, we manage about a 50% survival. On the other hand, even the early tumors diagnosed by mammography have sometimes metastasized. Hence we are looking for perhaps a 25% improvement in total survival. Secondly, the historical material with which we shall be comparing these patients' experience is really not very satisfactory. There are, of course, numerous large hospital series and there is the End Results compilation, but the End Results data rest on a complicated calculation of "relative survival". In all, it seems to me extremely difficult to construct any satisfactory comparison between the experience of these women in five years' time and the comparison data derivable from other sources.

Objective #5 - "To evaluate the effect of ACS literature on the teaching of breast self-examination in an effort to find out if women continue self-examination of the breast, and if they do not, then why?"

This is an important but difficult question which properly belongs in the field of the educator and the social scientist. It is not at all simple to sort out the relationship between what people say they do and what they actually do, or to establish valid reasons for behavior. I would guess that this is simply not worth doing unless there is in the project the resources for a proper state of the art study of these essentially psychological and sociological questions. This is not to suggest that contemporary social scientists have all the answers, but at least they do know a lot more about this area than physicians or statisticians.

Objective #6 - "To try to define again high risk groups for breast cancer".

This will be feasible, as there are internal comparisons that can be made betwen the women who did and did not develop breast cancer. However, this is a byproduct of the main objective and without the introduction of new variables is likely merely to confirm our current knowledge of the influence of early pregnancy, etc. Much more sophisticated studies addressed to this problem are in progress in California and elsewhere at the present time. In your manual it then follows by saying, "Success in the project will be measured by:

Criterion #1 - "Number of non-palpable breast cancers detected".

A number, probably quite large, will be produced at the end of the project without a context. It will not help in the debate as to whether we should go for a national system of early breast cancer detection through these methods or whether there are better uses for our resources.

Criterion #2 - "Prolonged life (i.e., 5-year survival without evidence of disease) of patients with non-palpable breast cancer (compared to historical studies of women with palpable breast cancer)".

You will also be able to compare your non-palpable tumor patients with the HIP patients in the same situation: The trouble again is going to be your comparisons with the other studies.

Criterion #3 - "Number of women screened in these projects who continue self-examination of the breast (as compared to historical studies)".

Presumably you will have a system for picking up the women who find tumors in between their routine thermographic/mammographic sessions and comparing them with women who are found at the sessions themselves. The design here is really rather complicated, with its comparison of improved breast cancer detection by the women themselves, using ACS methods, and the detection of the early tumors by more technical devices. Surely, only a few women are going to be sufficiently unlucky to have tumors which are undetectable by clinical examination, thermography and mammography, and then develop a tumor which they can palpate before their next go-round with the major system. Such women may have disastrously fast-growing tumors and their experience may reflect very badly on the simple ACS method. I suspect that the ACS techniques and mammography/thermography cannot be compared in the same population of women at the same time, and it does not sound to me as if the problem has been worked out by those who designed the overall study.

Criterion #4 - "Mortality rates of women with non-palpable breast cancer as compared with women with palpable tumors (historical data)".

This really runs into Criterion #2 and is subject to the same difficulties.

There are, besides the problems raised by the objectives of the study and its criteria for success, a host of very difficult but technical problems involved with the collection of data and the design of suitable forms for its recording. It seems to me that the coordinating center is going to have a very large job indeed to design data collecting instruments which are adequate for the very severe task, and to insure that the information that is desired really does come in a complete manner and is analyzed properly. These things sound simple enough but all recent experience of cooperative clinical trials, etc., underlines how difficult they really are, particularly with inexperienced institutions.

Whatever happens, this center is bound to be the center of controversy and it will receive a highly critical reception when its results are published. If it supports the practice of mammography and thermography, it is going to necessitate very large costs in money and in scarce resources of trained personnel. If, on the other hand, it suggests that these techniques are of comparatively small value, it is going to be attacked by the dedicated proponents of the methods. There seem to me to be two things that could be done even at this late stage to improve the designs and make it less liable to be destroyed by its critics. Somewhere we should aim to reach a substantial proportion of the women at risk in a defined area, and we should acquire some internal control data on the experience of women who did not have these sophisticated methods of early detection.

I am sorry to be so critical of this study, whose design I have only seen from a peripheral point of view. But it does seem clear to me that if the design is not materially modified and strengthened, the long term outcome is not going to be good. I have tried to indicate ways in which I think that this could be done, but the precise changes made are not important. The important thing is that real demonstration be developed, which will stand up to the scrutiny of expert opinion when it is eventually published.

Sincerely yours,

J. A. H. Lee

John A. H. Lee, M.D.
Professor

JAHL:nn

Mr. ROGERS. I commend you for that.

Dr. Carter.

Mr. CARTER. Thank you. Your testimony bore out a great deal of what we have been saying this morning rather strikingly, I thought.

Has mammography caused increased breast cancer?

Dr. BAILAR. I believe that it has not caused any detectable increase at this point, but that there will be an increase in years to come because of the latent period between exposure and the occurrence of cancer.

Mr. CARTER. Is that the reason why this program has been altered—because of the possibility of that happening?

Dr. BAILAR. The expectation?

Mr. CARTER. Yes.

Dr. BAILAR. I believe it is.

Mr. CARTER. Have you suffered from whistle blowing yourself?

Dr. BAILAR. I would have to say that, yes, I have, on a temporary and short-term basis. I do not believe that in the long run my career or my reputation have been permanently damaged.

Mr. CARTER. I noticed that on making diagnoses of the minimal cancers, there was an error rate of 10 percent among the minimal, but not as a whole. It was 11 percent to be exact. Really, I don't think that in handling the radiation over the years that we have ever fully understood what it might do until recently, until the past 20 or so years. Actually, we have been handling a power, the limits of which were unknown to us, including its capacity to cause harm.

I want to thank you for your very good testimony.

Dr. BAILAR. Thank you.

Mr. ROGERS. I notice you feel that 65 percent of the equipment in use operates at radiation levels, exposure levels higher than should be obtained with the best technology?

Dr. BAILAR. Yes.

Mr. ROGERS. That seems to be somewhat at variance with the impression given, I think by some statement by Dr. Pomerance. Perhaps you can comment.

Dr. BAILAR. Yes, the current guidelines call for exposure levels less than 1 rad or 1,000 millirads. I believe there was a statement this morning that in the BCDDP the xeromammography process was operating at an average of 570 millirads which is well under the 1,000 millirad limit. On the other hand, the film-screen combination equipment in that same program, using an entirely different method of producing an image, is operating at an average of 71 millirads which is approximately ⅛ of that with xeromammography. While all of these machines are below the 1,000 millirad limit, I believe that it would be a good thing to keep the doses as far below that limit as possible. Seventy-one millirads is a lot better than 570.

Mr. ROGERS. You say there were really widespread, if not publicized, doubts about mammography as early as 1973?

Dr. BAILAR. Yes.

Mr. ROGERS. What was the response of NCI or the American Cancer Society to this, or was it even discussed?

Dr. BAILAR. Mr. Chairman, it is very hard to respond to that except to say that there was virtually no response. It is not that those who were raising questions got answers they found to be unsatisfactory. We did not get answers at all. There were perhaps one or two memos on the matter that were quite unsatisfactory, but there was really no careful, thorough examination of the various problems and issues that had been raised.

At one point in I believe March of 1973, I made a very strong suggestion to the person then Director of the National Cancer Institute that someone be appointed to do exactly this. I had verbal agreement with that, but nothing ever happened.

I may say that I continued personally to raise questions, to express my doubts for a period of another couple of years, and nothing happened, nothing at all, sir, until the matter became public.

Mr. ROGERS. Well, now, the New York HIP study indicated there was a problem for age 50 and under, did it not?

Dr. BAILAR. The HIP study did show that there was a distinct reduction in breast cancer mortality for women over 50. It was in a sense, you could say, inconclusive with respect to women under 50.

It showed no benefit whatever, but the number of women expected to get breast cancer in that age was small enough that one could not say definitely there was no benefit.

Mr. ROGERS. The first guidelines put out permitted under 50?

Dr. BAILAR. Yes. They not only permitted, but they assumed it would be done.

Mr. ROGERS. They encouraged it. About when did that start?

Dr. BAILAR. With respect to the BCDDP, that was the initial design of the program. As far as I can remember, there was no major difference in the way women were screened depending on age.

Mr. ROGERS. At about what time was that?

Dr. BAILAR. The first of the centers must have been in operation by late 1973, perhaps early 1974. The dates escape me, sir.

Mr. ROGERS. Then they began getting a little concerned and put out some additional guidelines?

Dr. BAILAR. That was not until the BCDDP was in full operation, all 27 centers. That came along perhaps some 18 months later. My first public statement on this was 18 months later in May of 1975.

Mr. ROGERS. Now, they changed the guidelines then?

Dr. BAILAR. Not immediately, sir.

Mr. ROGERS. When were they changed?

Dr. BAILAR. I believe it was August of 1976.

Mr. ROGERS. Did the American Cancer Society oppose those changes or give any opposition to any changes?

Dr. BAILAR. I was, of course, not affiliated with the program at that time and it would be an understatement to say that communication was poor. Things have been reported to me third and fourthhand to the effect that the American Cancer Society was very strongly opposed to any change in the guidelines, to any restriction of screening for women under 50.

Mr. Rogers. Why do you think they would have taken that position?

Dr. **Bailar.** It is hard to say, sir, why any large agency would do such a thing. Outsiders can only guess, but I think it may be partly a matter of institutional inertia. It may be partly a matter of concern over their relations with the public which, of course, is very important to any agency dependent upon the public for contributions.

It may have been concern over the possible long-term effects on women who had been screened and would at some future time develop breast cancer. There are going to be a lot of them, sir, even if the radiation has no effect. Seven percent of the American women get breast cancer. Even if the radiation in this program were without effect, we would expect about 7 percent of the screenees to get breast cancer.

Mr. **Rogers.** Without that exposure, what would you anticipate the rate to be?

Dr. **Bailar.** I have not reviewed the figures for some time, but my feeling is that—if I remember the figures correctly—each REM of screening of 280,000 women, using the techniques in use at the time I made those criticisms, would produce over a lifetime, I think, something on the order of 50 breast cancers.

Mr. **Rogers.** Now did the American Cancer Society either formally or informally voice concern or even opposition to your comments on the program?

Dr. **Bailar.** Yes, sir. There was, again, I think, a great deal of activity that was not fully reported to me, but I have heard third and fourth hand that there were many comments and criticisms, suggestions that I be officially silenced in one way or another.

Mr. **Rogers.** Did you have your job change at that time?

Dr. **Bailar.** No, sir. The job change occurred at my own request in late 1973, when I found that I could no longer effectively work in the cancer control program because of concerns over this issue.

I asked for a transfer to another position. I moved then to the Journal of the National Cancer Institute, where I still am.

Mr. **Rogers.** Were you ever contacted personally by anybody from the Cancer Society on your feelings or your comments?

Dr. **Bailar.** No.

Mr. **Rogers.** What about the urgent bulletin we discused this morning?

Dr. **Bailar.** There was some discussion this morning about the circumstances in which this came to be issued. The guidelines I mentioned were changed in August of 1976 at the insistent urging, I understand, of members of the American Cancer Society who then signed the revised guidelines that went out to the 27 centers.

Now, at the same time it seemed to me from the outside that they almost immediately began trying to attain further weakening of those guidelines.

You heard this morning about the editorials in CA, which is sent free of charge to every physician in the country. You heard about the article in the Reader's Digest. There were private conversations with the project directors in these 27 centers. I see this urgent message as fitting into the same pattern of trying to attain some weakening of even those very loose guidelines.

Mr. **Rogers.** Was that just the New York group, or was it the American Cancer Society?

Dr. **Bailar.** I understand, sir, that the urgent message was drafted for initial use by the New York group, but that it was discussed in the national office, which happens also to be in New York City. It was then published and distributed in something like 20,000 or 30,000 copies by the New York Division, acting semi-independently with encouragement of people in the national office, to see whether it would fly.

I obtained a copy of that almost immediately after it was made public and wrote a memorandum, a critique, for the Deputy Director of the Cancer Institute, that said, in effect, "The ACS has insisted on changing our guidelines, why don't we try to have some effect on theirs?"

The story is further confused by the fact that the Guttman Institute mentioned at the bottom of the urgent message has several different sources of financial support. Part of the money comes from, and came from, the National Cancer Institute. Another part of it came from private sources, so that any woman who was ineligible for screening under NCI guidelines could still be screened at the Guttman Institute. It was just a matter of what set of books she was entered in.

Mr. **Rogers.** Did the NCI object to that bulletin at all?

Dr. **Bailar.** I do not know of any official objection that was raised, although, as I said, I suggested that there be such.

Mr. **Rogers.** The committee will stand in recess until after our next vote.

[Brief recess.]

Mr. **Rogers.** The subcommittee will come to order, please. I just have one or two more questions.

The Beahrs report was scheduled, I think, to be finished and reported out some time ago. Dr. Fredrickson said it would be published, as I recall, last December.

Dr. **Bailar.** Yes.

Mr. **Rogers.** I understand a final report was submitted and then the authors asked that a final report be changed. Could you comment on that? Do you have any knowledge of that?

Dr. **Bailar.** The report presented at the consensus meeting in September was not, as I recall, submitted as anything less than a final report. It was not labeled preliminary draft or anything of that sort. Shortly after the consensus meeting there was some concern on the part of some of the committee members that perhaps—well, I do not know, perhaps they thought they got more reaction than they expected and had to tone things down, or whatever, I do not know. But after suggesting that they might alter the report, and finding that that would not be a good way to proceed, the committee has been working on what is to be an addendum.

I might say here, sir, that I am in a sense wearing two hats because there has been some discussion of submitting this report to the Journal for which I am editor. Since December I have received frequent statements that the addendum was almost finished—1 week, 10 days, perhaps 1 month away—but I heard again this morning it is still 1 month away.

Mr. **Rogers.** Dr. Upton, could you comment on that?

Dr. **Upton.** I had spoken yesterday with Dr. Beahrs about this very report, and he assures me that he and Mr. Shapiro of the working group were going to confer last evening and attempt to put their final draft into the mail to the members within the next several days so that within a couple weeks presumably we will have the final report.

Mr. **Rogers.** What was the trouble with the delay? Because I thought it was all set.

Dr. **Upton.** I think when the committee made its report last August or September, they asked to be allowed to continue their work for an additional period of 6 months or so. One of the issues that the committee did want to resolve was in fact this set of 66 minimal cases in which the original pathologist's diagnosis of cancer was not verified. It became apparent after the report was submitted that not all of the case materials had been examined, and the committee wanted to be sure it had an opportunity to look in detail into all of the available material in those cases.

Mr. **Rogers.** Have the other 86 slides been submitted?

Dr. **Upton.** Those other slides, to my knowledge, have not been reviewed by the Beahrs working group but they are to be reviewed by Dr. Hartman and another pathology review group.

Mr. **Rogers.** Have they been submitted, do you know?

Dr. **Upton.** Mr. Chairman, it is my understanding that all of the cases diagnosed as cancer in the BCDDP are to be reviewed by Dr. Hartman and a committee of pathologists, and that committee is in effect proceeding with the review in question.

Mr. **Rogers.** I understand that. I am asking about the 86 slides that no one can find, have they yet been submitted?

Dr. **Upton.** To my knowledge, the Beahrs working group has not received those, nor does it wish to receive them now.

Mr. **Rogers.** Has anybody received them at the National Cancer Institute?

Dr. **Upton.** I cannot answer that.

Mr. **Rogers.** Does anybody know?

Dr. **Bailar.** I understand, sir, that some of the additional cases were submitted to the pathology review group, that they found additional lesions that they considered entirely benign, but I do not know how many were submitted or how many benign, so the number now would be somewhat larger than 66.

Mr. **Rogers.** Could we have that for the record, whether or not they have been submitted? I think it would be well to have numbers, and who has not yet submitted the slides.

[The following information was received for the record:]

When the Pathology Review Sub-Group of the Beahrs Committee began their analysis, they identified 592 cases among the cancers reported that fit their criteria for the group of cases they wished to review, i.e., the minimal cancers—those which were invasive and less than 1 centimeter in size and those which were non-invasive. Pathology slides and information were requested for those 592 cases, of which 506 were received in time for the review to take place. It was the opinion of the biostatisticians and epidemiologists in the Beahrs group that the 506 cases for which material was received would be a statistically valid sample to exclude any bias that might be introduced from the remaining 86 cases for which no pathology information was received. Therefore, further effort was not made to collect the remaining 86 cases because of the press of time for completion of the review. In 1976, a Pathology Quality Control review had been initiated for a retrospective review of the pathology obtained through the BCDDP. All information on pathology comes on a voluntary basis from the medical community to which screenees were referred for further consultation when positive findings were observed. This information is obtained from hundreds of hospitals and there is no obligation to submit the information except for the interest in contributing to the knowledge on breast cancer and to provide a valuable information resource for learning about the pathology of the disease. The retrospective review is still in progress under the leadership of Dr. William Hartmann of Vanderbilt University. That review will continue with the major objective of contributing to the fundamental knowledge of the pathology of breast cancer and developing an information resource which will be valuable for all pathologists who may have to be involved in the diagnosis of breast cancer, particularly in cases that have been detected early in the stage of the disease and that are difficult to interpret in the continuum between benign lesions and those that are unequivocally malignant.

Mr. ROGERS. Dr. Carter.

Mr. CARTER. With respect to the 66 women with benign slides, have they been informed of their condition? What has happened to them? Their tissue slides were first diagnosed as being cancerous but then later review showed them to be negative. Can anyone give a history of what happened to these 66 women?

Mr. BAILAR. May I defer to Dr. Upton.

Dr. UPTON. Dr. Carter, you asked about those cases. I do have a report from the Beahrs working group. Again, we have not received their final report but the latest information we have is as follows: As Dr. Bailor mentioned, 2 of the 66 cases were included in the group by accident to begin with, and should not have been included, so that the correct number is actually 64 cases in which the original diagnosis was cancer, and the working group was unable in its preliminary efforts to confirm that diagnosis.

The working group has since been able to confirm 16 of the cases based on additional slides that were not available to it last summer.

Mr. CARTER. Sixteen as being positive?

Dr. UPTON. Sixteen as being positive. So that leaves now 48 cases which were not confirmed.

In 11 of the 48, the patient was treated by biopsy only. There was apparently enough of a question in the minds of those who treated the patient originally so as not to warrant the mastectomy. That leaves 37 cases in which a mastectomy was performed and in which the original diagnosis was not confirmed by the review group.

In 30 of those 37 cases the operation was performed in two stages. A biopsy was carried out, a diagosis of cancer made, and then at some interval of days to months actually a second operation, a mastectomy, was performed.

Mr. CARTER. Radical mastectomy?

Dr. UPTON. In a number of those cases the operation was radical. I do not have that information in front of me. But in only a few of the 30 cases was there a radical. It turns out that in a number of instances the original pathologist—actually, in 15 of the 30 cases—the original diagnosis was confirmed by consulting pathologists, so that there was an opportunity to verify to that degree the original opinion before a decision to do a mastectomy.

[The following information was received for the record:]

According to the latest information available from the Beahr Working Group, three of the 66 women underwent radical mastectomies.

Mr. CARTER. Wait a minute. Let's go over that rather carefully. You say for some reason 2 of the 66 got into another group and were supposedly checked and found free of cancer?

Dr. UPTON. Sixty-six specimens were submitted to the working group with the diagnosis of cancer, and in two of those instances the specimens should not have been submitted to begin with. They were not properly classified.

Mr. CARTER. Yes.

Dr. UPTON. They represented extraneous lesions that really should not have come for examination.

Mr. CARTER. And 16 more——

Dr. UPTON. Of the remaining 64 cases, 16 have since been confirmed by the Beahrs pathology subgroup.

Mr. CARTER. Confirmed as——

Dr. UPTON. Confirmed as malignant, as cancer. So that leaves, as I indicated, 44 cases in which——

Mr. CARTER. Forty-eight.

Dr. UPTON. Forty-eight cases in which the Beahrs working subgroup was unable to confirm the original diagnosis. In 11 of the 48 cases there was a biopsy alone, there was no mastectomy, there being in the minds of the surgeons who treated the patient originally been a question about the significance of the diagnosis, so that there was no decision to go ahead and do a mastectomy.

Mr. CARTER. Of those 11, have these women been told of the recent findings?

Dr. UPTON. We have transmitted to each of our projects the information received from the pathology review group, and we have requested each project to notify women that the information is available to them. The information has been given to their physicians, with the request——

Mr. CARTER. Eleven of the 48 were not operated except for a biopsy?

Dr. UPTON. That is correct.

Mr. CARTER. Then the other 37——

Dr. UPTON. In the other 37 there was a mastectomy following the biopsy, and in 30 of the 37, the interval between mastectomy and biopsy was a matter of days to months.

Mr. CARTER. Why?

Dr. UPTON. Why such a long interval?

Mr. CARTER. Yes, sir. Usually, you and I know, when there is a lesion in a woman's breast the physician takes a biopsy, a frozen section. Then the pathologist reports immediately and a radical mastectomy is performed if the section was malignant.

Dr. UPTON. Yes, that has been the traditional approach, Dr. Carter. I think today, particularly with lesions such as these—they represent a very special and difficult category of lesions because they are small, they are not the kind of lesion that most pathologists have seen before; they are tiny lesions about which there is understandably some question and some difference of opinion as to interpretation.

Mr. CARTER. Yes, sir.

Dr. UPTON. So with this class, when there is such a degree of uncertainty, it is advisable for time to elapse to allow appropriate consultation—based on the availability of permanent, well stained material, and not simply the frozen section material—and also to confer with the woman herself. Today we see a trend in the treatment of breast cancer, generally, to permit the patient to have the biopsy and then to confer with the surgeon about the proper follow-up treatment before proceeding with a decision for mastectomy.

Mr. CARTER. We have the 11 taken care of. How about the other 37?

Dr. UPTON. In the other 37 cases it turns out that there was a lapse of time between the biopsies and the mastectomy, and in at least 15 of those cases there was consultation among outside pathologists about the interpretation of the original lesion. In only seven cases was the mastectomy carried out on the same day as the biopsy, and in two of these one-stage mastectomies, the original diagnosis was supported by the project pathologist. In three of the cases the project pathologist differed in interpretation with the original pathologist, and in two cases the diagnosis was based on the frozen section material and no permanent slides were available for reinterpretation.

So I think we can argue that in the 37 cases there remain only 5 cases in which there was not at least one opinion by a consultant in agreement with that of the original pathologist.

Mr. CARTER. We discussed 15 there but we did not consider the other 22 in that group. Twenty-two of those women who were operated on had radical mastectomies with their slides being negative. Is that not correct?

Dr. UPTON. It is my understanding, Dr. Carter, that in 15 of the 30 cases in which there was a two-stage mastectomy there was consultation in arriving at the diagnosis.

Mr. CARTER. Do you mean that this figure of 66 is incorrect? Do you mean that actually most of them were positive, according to what you have said?

Dr. UPTON. What I am trying to say, Dr. Carter, is that the 66 cases represent a very difficult class of lesions; that the Beahrs working subgroup in pathology has, with examination of additional material, arrived at the same diagnosis as the original pathologist in 16 out of the 66. So 16 cases are now confirmed and 2, as we indicated, were misclassified to begin with in that group.

Of the 30 in which there was a 2-stage mastectomy, there was a consulting opinion on at least 15 of them.

Mr. CARTER. On 15 there was no consulting opinion, then?

Dr. UPTON. I regret to say I do not have the complete data in front of me.

Mr. CARTER. Then we have 15 women who, according to a group of eminent pathologists, underwent radical mastectomies. What does that operation include, Dr. Upton? Let's go through that.

Dr. UPTON. A radical mastectomy involves removal of the breast tissue itself, the muscles.

Mr. CARTER. And does it include getting the nodes out of the maxilla, if there are any?

Dr. UPTON. Yes.

Mr. CARTER. Usually you do it when you cut clear through; is that correct?

Dr. UPTON. I have not——

Mr. CARTER. I understand.

These 15 women have lost their breasts and their sense of beauty and dignity and wholeness. Mistakes were made in those cases, and yet they were operated on.

Dr. UPTON. As you know, Dr. Carter——

Mr. CARTER. They were operated on on the wrong basis and actually if there is a malpractice liability——

Dr. UPTON. As you know, Dr. Carter, the screening program has been involved in the detection of suspicious lesions in the breast. These patients have been diagnosed and treated by their private physicians. We have conveyed all of the information we have received to the projects with the request that the project inform the women that the information is available to them through their physicians.

Mr. CARTER. Has it gotten to these women?

Dr. UPTON. It has been given to the physicians, and I assume that the physicians have informed them.

Mr. CARTER. You assume that. That does not go far enough. You have to get down to each patient and inform that patient, I should think, as a matter of honor, honesty, decency, and humanity.

Dr. UPTON. I am told by colleagues in the professional community that these in fact are not our patients, that we are intruding ourselves into the physician-patient relationship. We supply the money for the detection of a suspicious lesion in the breast. We are not involved in the final diagnosis and subsequent treatment of that lesion.

Mr. CARTER. Who is liable in the cases of these women? At least 15 of them, it seems to me, have an excellent malpractice case against someone. Who is liable for that, Doctor?

Dr. UPTON. I think one of the issues, Dr. Carter, is really what is the correct interpretation. The Beahrs working group did not arrive unanimously at the same interpretation in all cases. There was disagreement among the members of that working group. I think that the question of liability is a very difficult one here, and I certainly am not an expert in the matter.

Mr. CARTER. You are a wonderful person, a fine gentleman. But actually the testimony states that a group of eminent pathologists concluded that 66 were entirely benign. I will give you the right to say some were examined by other pathologists and they may have found some of them that way. But even at that, you still have a group of women who have had their breasts removed, who have been crippled, I am afraid.

Thank you, Mr. Chairman.

Mr. ROGERS. Let me just ask a question. It is my understanding that some of these contracts for the screening program were not advertised and did not go through the procedure of competitive bidding. Has that been looked into?

Dr. UPTON. I will have to defer that question to Mr. Costlow, Mr. Chairman.

Mr. ROGERS. Certainly.

Dr. COSTLOW. My information—I perhaps cannot be very accurate since I was not involved at the inception of these contracts—but I understand that there was a competition and there was a selection process.

Mr. ROGERS. Was it advertised?

Dr. COSTLOW. Yes.

Mr. ROGERS. In other words, all of these were advertised, there was a competitive bidding procedure?

Mr. Costlow. Yes.

Mr. Rogers. Dr. Bailar, did you have some comment?

Dr. Bailar. Yes, Mr. Chairman. I was involved in the program myself at that time. It was some time before Mr. Costlow came to the Cancer Institute. I believe it is correct to say that these were not advertised and that it was not competitive bidding in the usual sense.

The American Cancer Society took on the task of generating interest in this program, of stimulating the submission of proposals which were then initially screened by the American Cancer Society to determine which ones they felt would be most proper for further consideration for funding.

Mr. Rogers. How much Federal funding was involved using that procedure?

Dr. Bailar. At that time it was about 80 percent Federal funding.

Mr. Rogers. This would have been what amount of money?

Dr. Bailar. About $6 million a year.

Mr. Rogers. Is that procedure still going on? Is that what you call competitive bidding?

Dr. Costlow. Oh, no, sir. The basis of my answer was in going over some of the files originally when I first got into this, was there were several institutions listed there as having participated in what I assume was a competition that were not selected, that is, ultimately did not become one of the 27 centers. That is really the only basis I had to make my statement since I was not involved in the beginning.

Dr. Bailar. Dr. Costlow is correct about that. There were about twice as many proposals submitted as were eventually funded, but this never went through the formal procedures of government advertising that are familiar to us.

Mr. Rogers. I presume, Doctor, you will want to look into that to make sure the procedures are correct.

Dr. Upton. Yes, indeed, Mr. Chairman.

Mr. Rogers. Do we know what criteria the ACS used for selecting these people?

Dr. Bailar. Those criteria were written down. I have a copy but I do not recall them.

Mr. Rogers. If you do have them, we would appreciate them being furnished.

[The following information was received for the record:]

Evaluation of Breast Cancer Demonstration Projects

CRITERIA OF EVALUATION

TECHNICAL ABILITY	SCORE
Mammography	30
Thermography	20
Physical Examination	30
Pathology Examination	20
Total	100
ORGANIZATIONAL ABILITY	
Ability to Secure Screenees	25
Ability to Process Screenees	15
Ability to Obtain re-examinations (reg.)	20
Ability to Obtain re-examinations (spec.)	10
Ability to fill out Forms, accurately and promptly	20
Cost of Examination	10
Total	100
COOPERATION WITH THE AMERICAN CANCER SOCIETY	
Ability to obtain Volunteers	15
Ability to Use Volunteers Well	10
Ability o6 Acs to Publicize Projects	20
Ability of ACS Volunteers to Persuade Screenees to Return for Re-examination	40
Overall Cooperation of Project and ACS	15
Total	100

BEST COPY AVAILABLE

Evaluation of Breast Cancer Demonstration Projects.

General Projects will be evaluated from a number of different view points, and from materiel or information provided from a number of sources such as; 1. Statistical Center (SC), 2.Project Officer (PO) evaluation.,3.Site visit reports, 4.Project progress reports., 5.American Cancer Society Reports.

It is suggested that site visit committees for these projects should have available as much materiel as possible prior to the site visit. This materiel would be gathered by the Project Officer from the Statistical Center (SC)(this might be data concerning quality control, forms, promptness of replies and submission of records etc.); from the Project Officer, (Progress Reports, Finances, etc.); from the American Cancer Society,(Local Acceptance,Cooperation, Physicians acceptance, Impact on Community etc.) and sent to site visitors prior to the visit. The problems of projects should be sought as well as their successes.

Site visitors and reviewers should recognize that both the ACS and the NCI are anxious to see that these projects attain their goals. Every effort should be made to assist each project in attaining its goal to demonstrate the value of screening in the detection of 'early' or occult breast cancer. Solving problems may be of greater value than praising excellence in the evaluation of the practical problem that exists. Evaluators shou recognize that these are not 'research projects' but are in reality 'demonstration projects' that will 'demonstrate' that screening of the breast can be applied to large segments of the female population. This is an effort to improve the existing situation and to extend good diagnostic methods to women not now benefitting from these methods.

TECHNICAL ABILITY

Ability in this sector should be judged on the qualifications and performance of the persons involved and on their willingness to cooperate in studies of the recognition of breast cancer and in quality control studies. Are mammograms, thermograms, physical examinations and pathological examinations superior, adequate or inferior? Since expertise in these areas was sought in the original applications it is anticipated that this area would result in the least number of debates. If any projects are judged to be inferior the causes should be sought and corrections made in a reasonable length of time. Specific problems should be searched for and a solution suggested.

Technical ability in all four (4) modalities will be evaluated but mammography and physical examination are weighted as of greater value than thermography (as yet unproven) and pathology (assumed to be reasonably standard). Excellence of films, readings, double readings, cooperation and the interest of participants are all to be considered in scoring in this area.

BEST COPY AVAILABLE

ORGANIZATIONAL ABILITY

Generally this category of evaluation involves the ability of each project to secure candidates, process them, fill out forms accurately and promptly and to retrieve screenees. 'Regular' screenees are those who should return annually and 'special' screenees are those who should return because of technical errors in examinations, suspicious or for other reasons in less than one year from an examination. Ability to follow patients involves mechanisms for seeking out those who fail to return by usual recall methods. Does a project have unique methods of securing recall of patients?

All of these operations involve an evaluation of forms and how well they are filled out and how many errors exist. Cooperation with the SC as well as with the PO is vital in all of these areas.

Recall and management of screenees with suspicious or positive findings is vital to the success of the projects.

COOPERATION WITH THE AMERICAN CANCER SOCIETY

Can projects secure volunteers who actually aid in the function of the projects? Do volunteers take histories, file records, assist in follow-up? Are they used uniquely in some manner? Is the ACS publicity Unit used effectively to publicize the projects? Can ACS volunteers exert a special effort to obtain the return of screenees who do notwHich to return following the usual recall measures? Is this in truth a 'joint project' in which the breast unit works with the ACS unit for purposes of health education, re-assurance of negative cases and prompt management of suspicious or positive cases?

Mr. Rogers. Thank you so much for your presence today. We are grateful to you for your testimony.

The next witness will be Dr. William D. Rowe, who is the Deputy Assistant Administrator for Radiation Programs, Environmental Protection Agency.

Dr. Rowe, we welcome you to the committee. Your statement will be made a part of the record without objection, and you may proceed as you desire.

STATEMENT OF DR. WILLIAM D. ROWE, DEPUTY ASSISTANT ADMINISTRATOR FOR RADIATION PROGRAMS, ENVIRONMENTAL PROTECTION AGENCY, ACCOMPANIED BY JAMES E. MARTIN, PH. D., DEPUTY DIRECTOR, CRITERIA AND STANDARDS DIVISION, OFFICE OF RADIATION PROGRAMS; AND DEVAUGHN R. NELSON, FEDERAL GUIDANCE BRANCH, DIVISION OF CRITERIA AND STANDARDS, OFFICE OF RADIATION PROGRAMS

Dr. Rowe. Mr. Chairman, I will try to paraphrase my statement, if I may. I will also submit a copy of the Federal guidance on medical X-rays approved by the President. [See p. 1135.]

Mr. Rogers. Without objection, it will be made a part of the record.

Dr. Rowe. Since this is our authorizing committee, I am sure you are aware of the responsibilities given to us when EPA was set up due to the transfer of the Federal Radiation Council authority for radiation protection.

This authorization, which provides for advice to the President, gives us an overall overview responsibility for all matters pertaining to radiation.

In 1974, in trying to exercise these responsibilities, we came to the conclusion along with the recommendation of the BEIR committee—in their 1972 report—that the largest source of manmade radiation was from the medical X-ray area. We felt that while we had begun to do considerable work under this authority in the nuclear and other fields, we could not ignore the medical radiation problem, at least for diagnostic X-rays.

At that time we undertook an effort to try to discover what the problems were and what we could do about it. In the spirit of the former Federal Radiation Council, we established an interagency working group so we could have all the agencies involved. We had tremendous participation from the three services and the VA and their radiologists, their physicians and dentists working closely with us as we developed our information.

As you may well be aware, our butting our nose into these matters is not always well taken. In fact, we had, I would say, pretty much of an uphill fight getting into this area, even though our authority only covers Federal facilities.

We have no authority in the private sector. This gave us certain advantages because of the fact the doctors and physicians and dentists involved in the public sector are not faced with third-party problems, nor are they faced with the problems of trying to make direct profits in their operations. So they worked with us to do what could be done to assure that patients get the benefits of X-rays for diagnostic purposes, but to do so with minimum exposure.

In carrying this out, one of our underlying philosophies was: In no way should we try to interfere with the doctor-patient relationship. I think the balancing of risks and benefits that must take place and should be made by the expert who is working with his patient and can best take these risks and benefits into account. There were three areas that we had to consider. The first, was when to prescribe an X-ray. The second, was if an X-ray was to be prescribed, how we could assure that the procedures were optimized in such a way that a particular patient would receive the least exposure to get the best X-ray. The third was to assure that the equipment used to get these X-rays was up to date and the best available.

In this latter case we were certainly aware, that standards for equipment were promulgated by the Bureau of Radiological Health. We used their standards as a basis for our guidance, and have in no way duplicated that effort.

As we proceeded, we came to the point that we realized that many of the things we were saying would certainly create a lot of concern in the medical and health care communities. So we opened our process to the public for comment and responded to all of the inputs received.

We can now look back at this guidance with some perspective and appreciate that it simply amounts to commonsense and good practice, but laying out the commonsense and good practice in such a way that it can be implemented.

At the time we started, it was not so easy to recognize what makes sense. But now that we have done it, I think it makes a significant improvement, at least, in the Federal sector. I hope you will keep in mind the fact that sometimes just getting commonsense on paper is, indeed, difficult.

Our basic guidance is based upon two principles; namely, that no necessary diagnostic procedure should ever be precluded, that is the doctor-patient relationship should not be infringed; and that the X-rays taken should be of proper diagnostic quality.

Further, that clinically unproductive examinations should not even be ordered, and that the amount of patient exposure should be minimized in taking X-rays. As obvious as these may appear, the task was to translate them into a set of guides that could be applied without adversely impacting medical practice.

It must be remembered that radiation diagnosis involves a complex system in which the patient is generally the only continuum connecting professionals and praprofessionals, many of whom do not relate directly to the patient: clinicians, technologists, radiologists—or some other diagnostician—medical physicists, and administrative staff, just to name some of them. The physical layout presented to patients receiving X-ray diagnosis is a maze, the focal point of which is the X-ray facility. The X-ray facility is interconnected to clinics from which patients come with requests for X-rays, a backroom where films are interpreted, rooms for preparation and dressing, a film processing room, and a loosely linked equipment service and maintenance capability. The action relays from one area to the other, and if all perform correctly, the patient will receive the proper diagnosis and only that exposure necessary for the diagnosis. In the formulation of the Federal guides an attempt was made to address the proper functioning of each component of the system and to set forth goals and principles that, if satisfied, would assure that necessary X-rays are obtained at minimum exposure.

GUIDES FOR X-RAY PRESCRIPTION

The first group of guides are designed to assure that proper prescription has taken place before a patient is X-rayed. They address the ingredients that:

General radiographic or fluoroscopic examinations should only be prescribed by licensable physicians, or, for specified limited procedures, physician trainees and allied professionals under their direct supervision; specialized procedures should only be prescribed by professionals with the special training required to interpret the results.

The objective of prescribing an examination should be to obtain diagnostic information of a specific kind based upon symptoms that have been clinically evaluated and to communicate this information to the X-ray facility so that the X-ray diagnostician can assume responsibility for providing the diagnosis in the most efficacious manner, deleting or adding projections as appropriate, and taking special precautions for pregnant or possibly pregnant patients. Diagnostic information from X-ray examinations leads to direct medical benefits to the patient. An example of unnecessary but prevailing practice is skull examinations in trauma cases. Such examinations are usually not warranted since the patient will not derive medical benefit as the result of an altered treatment.

Screening and routine examinations in which patients do not receive a prior clinical evaluation should not be performed unless prior exception has been made for specific groups on the basis of a finding that the medical benefit exceeds the cost and radiation risk. This represents a reversal of a traditional view in medicine that established routines should not be discontinued unless proven unnecessary. Examples of such examinations that should not be performed unless such an exception is made include:

(a) Chest and lower back examinations in physicals or as a routine requirement for employment;

(b) TB screening by chest X-rays;

(c) Chest X-rays merely for hospital admission;

(d) Chest X-rays in routine prenatal care; and

(e) Mammography screening for asymptomatic women under age 50, unless they have a personal or strong family history of breast cancer.

X-RAY FACILITY GUIDES

The next set of guides are directed to the X-ray facility itself to assure that it is in optimum order when a patient arrives to be examined. It is recommended that technique protocols be established to provide the most efficacious examination by stating the number and types of views for selected examinations, emphasizing that the number of "standard" examinations be kept to a minimum and that even these need to be periodically reviewed.

Proper equipment and quality control is recognized by everyone to be essential to quality radiography at minimum exposure. Specific guides address equipment, its performance, and the performance of associated materials. Key elements are:

All general purpose medical and dental X-ray equipment in Federal facilities should conform to Federal X-ray equipment performance standards.

All fluoroscopic equipment for Federal facilities should have image intensification, and fluoroscopy units for nonradiology specialists should have electronic image-holding features.

Photofluorographic machines should not be used for chest X-rays.

Quality assurance programs should exist in all Federal clinics using X-ray equipment for both equipment and materials, including operational procedures for monitoring films and reducing retakes.

QUALIFICATIONS OF OPERATORS AND EXPOSURE EVALUATION

The way examinations are performed plays an essential part in radiation protection of patients and depends upon proper training and performance of the operator. The guides also specify that:

Operators should possess qualifications identical or equivalent to those of recognized credentialling organizations, or national performance-oriented evaluation procedures.

Operators are responsible to prepare patients properly, to provide collimation and shielding (especially to protect the fetus and the gonads), and to select proper technique factors to minimize exposure and obtain quality X-rays.

Standard examinations should be reevaluated if they fall above specified numerical exposure guides.

This last guide addresses the overall system of equipment/material/operator performance by providing exposure guides—and I emphasize the word "guides"—for selected standard examinations that identify exposures that may be higher than necessary. This guide was based upon a recognition that although each X-ray is evaluated for diagnostic quality when it is read, the exposure required to obtain it is rarely, if ever, evaluated. The thrust of the guide is the need to evaluate each system to determine if exposures are as low as reasonably achievable without loss of diagnostic information. Exceeding the exposure guides indicates that the system should be examined to reduce exposure; achievable exposures can generally be well below the guides, and we believe they should be kept there whenever practicable.

DENTAL RADIOGRAPHY

Although most of the guides address both medical and dental radiography, certain of them are applicable to dental radiography specifically:

Prescription of dental X-rays should be made only by licensable dentists on the basis of clinical evaluation.

Performance of full mouth and routine X-rays should not be a routine part of preventive dental care.

Dental technique should use long collimators with paralleling technique and with the X-ray field kept as near the image receptor size as practicable.

In approving these recommendations, the President directed the EPA Administrator and the Assistant Secretary for Health to carry out programs to interpret and clarify them as necessary. To this end, we have formed a subcommittee of the Interagency Working Group on implementation of the guidance. This subcommittee is chaired by the Bureau of Radiological Health in HEW. We are also planning to make an annual report to the President on the status of implementation of the guides.

These guides are only a first step. Other things can be done in the future such as:

Guidelines for use of appropriate shielding or collimation should be formulated for examinations where reduced exposure of reproductive organs or the fetus can be achieved.

Exposure guides for some additional common examinations, such as mammography and panoramic dental examinations, could be clarified.

Guidelines for quality assurance in specific areas are needed; these could include automatic film processors as well as other equipment and procedures in radiology departments. The development based upon the BEIR report should be developed for the evaluation of current and future X-ray screening programs.

It is expected that HEW will take a leading role through our memorandum of understanding in undertaking these activities; to date they already have in progress programs in the first three of these areas.

There has been some question concerning the extent to which this guidance applies to activities of Federal agencies. The guidance was developed by Federal personnel who gave primary consideration to the proper conduct of radiation protection in Federal health care facilities, and it is applicable without additional consideration to such facilities. Application to other programs, such as research grants, contracts, and federally funded public health programs, is to a large degree a matter for the determination of each agency. They are the ones that are closest to the programs and know how these can best be applied. We expect that each Federal agency will use it as a basis upon which to develop detailed standards to meet its particular requirements.

In summary, we believe that the new Federal radiation protection guidance for diagnostic X-rays will lead to demonstration of significant reductions in exposure to diagnostic X-rays. It is our hope that this will become an important milestone in radiation protection and that this Federal example will provide the impetus for improved protection in the private sector.

Thank you. I will be glad to attempt to answer any questions you may have.

[Testimony resumes on p. 1140.]

[Dr. Rowe's prepared statement and attachment follow:]

STATEMENT OF
DR. W. D. ROWE
DEPUTY ASSISTANT ADMINISTRATOR FOR RADIATION PROGRAMS
ENVIRONMENTAL PROTECTION AGENCY
BEFORE THE
SUBCOMMITTEE ON HEALTH AND THE ENVIRONMENT
COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE
HOUSE OF REPRESENTATIVES
JULY 14, 1978

Mr. Chairman and Members of the Subcommittee:

I am Dr. William D. Rowe, Deputy Assistant Administrator for Radiation Programs. Mr. Chairman, we appreciate this opportunity to describe our activities and efforts to improve radiation protection for uses of radiation in the healing arts.

Introduction

As you are aware, Executive Order 10831 and the Atomic Energy Act of 1954, Public Law 86-373, (42 U.S.C. 2021 (h)) charge the Administrator of the Environmental Protection Agency (EPA) to "...advise the President with respect to radiation matters directly or indirectly affecting health, including guidance for all Federal agencies in the formulation of radiation standards and in the establishment and execution of programs of cooperation with States." These functions, which had been carried out by the Federal Radiation Council (FRC) from 1959 to 1969, were transferred to the Administrator by Reorganization Plan No. 3 in 1970.

The function of the FRC provides the central focus in the Federal government for policy leadership to assure protection of the public from radiation. In its exercise of this role, EPA pursues extensive interaction with other Federal agencies because we believe that Federal guidance will be most effective and gain the widest application and public acceptance when developed in cooperation with those agencies bearing direct responsibility for its implementation.

The recent EPA initiative to develop Federal guidance on diagnostic x-rays resulted in the first action on radiation protection of patients under this authority. One might ask why it has taken so long to address this problem. The pressing and highly visible issues of fallout from nuclear weapons testing, underground exposure of uranium miners, and occupational exposure all required consideration by the FRC on a high priority basis after its establishment in 1959, and only more recently has the significance of medical exposure become as well recognized. In 1972, the National Academy of Sciences Committee on Biological Effects of Ionizing Radiation made a number of recommendations on unnecessary exposure of patients. One of their significant findings was that "medical diagnostic radiology accounts for at least 90% of the total man-made radiation dose to which the U.S. population is exposed." More importantly, the

Committee recommended that "medical radiation exposure can and should be reduced considerably by limiting its use to clinically indicated procedures utilizing efficient exposure techniques and optimal operation of radiation equipment."

In 1974, the Administrator recognized that a unique opportunity existed in medical facilities operated by Federal agencies, where it might be possible to provide an example of what could be done, and he formed an Interagency Working Group on Medical Radiation was formed to assist EPA in developing Federal guidance for reducing exposure from diagnostic x-rays. The Working Group agreed that it was possible to reduce exposure from the diagnostic use of x-rays in Federal facilities. We formed subcommittees to examine factors to eliminate clinically unproductive examinations and techniques to reduce exposure when examinations are performed. We did not pursue a third area - equipment specifications - to any great extent, since x-ray equipment is subject to performance standards of the Food and Drug Administration. The reports of these subcommittees were made available for public comment (41 F.R. 10705 and 27998) prior to completion of a summary report by the full Interagency Working Group.

Recommendations based upon this report were proposed by EPA for public comment (42 F.R. 4884) on January 26, 1977. In addition, there was extensive formal review by the Public

Health Service and by other affected Federal agencies. After careful consideration of these responses final recommendations were formulated and a complete record, including a detailed response to comments, made available to the public. A joint recommendation by EPA Administrator Costle and HEW Assistant Secretary for Health Richmond was transmitted to the President. The President approved the first Federal radiation protection guidance for diagnostic x-rays and issued it in the Federal Register (43 F.R. 4377) on February 1 of this year. (See Attachment)

We have also entered into a memorandum of understanding with HEW (42 F.R. 5123) which established a formal mechanism for the continued development and implementation of Federal guidance in this broad area of mutual concern to our two Agencies. Thus, for this largest of the man-made sources of public exposure to radiation, we now have the basis for making significant progress in radiation protection. With the help of our Interagency Working Group and HEW's Bureau of Radiological Health, we are proceeding toward effective implementation of this guidance and we shall develop any necessary detailed implementing guidelines.

The Federal Guidance for Medical Diagnostic X-Rays

I would now like to describe some of the major features of the new guidance. As a preliminary comment, you may be struck by the fact that much of the guidance consist of simple common sense statements, and you may wonder why it is necessary to make them. I can only state that in this area such statements are necessary because they have often not been followed in the past, and merely getting them formalized should provide the basis for significant progress. What we have presented is expressed as a set of requirements for good practice. The guides were developed in conjunction with practicing radiologists and health physicists from agencies operating major health care programs. These included the three armed services, the Veteran's Administration, and HEW. It should be noted that in the Federal hospitals from which these experts come, problems associated with third party pressures for diagnostic x-rays, as well as the direct monetary reward for providing x-rays, are not present as they are in the private sector.

The guidance is based on two basic principles of radiation protection. These are: (1) that there should not be any man-made radiation exposure unless the benefits exceed the radiation risk and the cost, and (2) that for exposures justified by their benefit, every effort should be made to insure that radiation doses are as low as reasonably achievable.

Some basic preconditions were satisfied during the development of the guidance. The first two were: 1) that no necessary diagnostic procedure should ever be precluded, i.e., the doctor-patient relationship should not be infringed; and 2) that the x-rays taken should be of proper diagnostic quality.

Adherence to these first two principles would be understandable even without the presence of physicians on the working group, but was doubly so since they were present. But although these two principles were important, two others were equally so; these were: 3) that clinically unproductive examinations should not even be ordered; and 4) that the amount of patient exposure should be minimized in taking x-rays. As obvious as these may appear, the task was to translate them into a set of guides that could be applied without adversely impacting medical practice.

It must be remembered that radiation diagnosis involves a complex system in which the patient is generally the only continuum connecting professionals and para-professionals, many of whom don't relate directly to the patient: clinicians, technologists, radiologists (or some other diagnostician), medical physicists, and administrative staff, to name most of them.

The physical layout presented to patients receiving x-ray diagnosis is a maze, the focal point of which is the x-ray facility. The x-ray facility is interconnected to clinics from which patients come with requests for x-rays, a back room where films are interpreted, rooms for preparation and dressing, a film processing room, and a loosely-linked equipment service and maintenance capability. The action relays from one area to the other and if all perform correctly, the patient will receive the proper diagnosis and only that exposure necessary for the diagnosis. In the formulation of the Federal guides an attempt was made to address the proper functioning of each component of the system and to set forth goals and principles that, if satisfied, would assure that necessary x-rays are obtained at minimum exposure.

Guides for X-Ray Prescription

The first group of guides are designed to assure that proper prescription has taken place before a patient is x-rayed. This involves not only the determination that x-rays are required to diagnose disease or injury, but also decisions usually made by the radiologist conducting the examination, especially the number and types of views, since these determine the overall exposure the patient receives. There is too great a tendency to make routine both the examination to be prescribed and the number and types of views included. The essential ingredient in not over-prescribing is thoughtful action by qualified personnel; the guides address key points in this regard. They are:

- General radiographic or fluoroscopic examinations should only be prescribed by licensable physicians, or, for specified limited procedures, physician trainees and allied professionals under their direct supervision; specialized procedures should only be prescribed by professionals with the special training required to interpret the results.
- The objective of prescribing an examination should be to obtain diagnostic information of a specific kind based upon symptoms that have been clinically evaluated and to communicate this information to the x-ray facility so that the x-ray diagnostician can assume responsibility for providing the diagnosis in the most efficacious manner, deleting or adding projections as appropriate, and taking special precautions for pregnant or possible pregnant patients. Diagnostic information from x-ray examinations leads to direct medical benefits to the patient. An example of unnecessary but prevailing practice is skull examinations

in trauma cases. Such examinations are usually not warranted since the patient will not derive medical benefit as the result of an altered treatment.

- Screening and routine examinations in which patients do not receive a prior clinical evaluation should not be performed unless prior exception has been made for specific groups on the basis of a finding that the medical benefit exceeds the costs and radiation risk. (This represents a reversal of a traditional view in medicine that established routines should not be discontinued unless proven unnecessary). Examples of such examinations that should not be made include:
    a) Chest and lower back examinations in physicals or as a routine requirement for employment
    b) TB screening by chest x-rays,
    c) Chest x-rays merely for hospital admission,
    d) Chest x-rays in routine prenatal care, and
    e) Mammography screening for asymptomatic women under age 50, unless they have a personal or strong family history of breast cancer.

X-Ray Facility Guides

The next set of guides are directed to the x-ray facility itself to assure that it is in optimum order when a patient arrives to be examined. It is recommended that technique protocols be established to provide the most efficacious examination by stating the number and types of views for selected examinations, emphasizing that the number of "standard" examinations be kept to a minimum and that even these need to be periodically reviewed.

Proper equipment and quality control is recognized by everyone to be essential to quality radiography at minimum exposure. Specific guides address equipment, its performance, and the performance of associated materials. Key elements are:

- All general purpose medical and dental x-ray equipment in Federal facilities should conform to Federal x-ray equipment performance standards.
- All fluoroscopic equipment for Federal facilities should have image intensification, and fluoroscopy units for non-radiology specialists should have electronic image-holding features.
- Photofluorographic machines should not be used for chest x-rays.
- Quality assurance programs should exist in all Federal clinics using x-ray equipment for both equipment and materials, including operational procedures for monitoring films and reducing retakes.

Qualifications of Operators and Exposure Evaluation

The way examinations are performed plays an essential part in radiation protection of patients and depends upon proper training and performance of the operator. The guides also specify that:

- Operators should possess qualifications identical or equivalent to those of recognized credentialling organizations, or national performance-oriented evaluation procedures.
- Operators are responsible to prepare patients properly, to provide collimation and shielding (especially to protect the fetus and the gonads), and to select proper technique factors to minimize exposure and obtain quality x-rays.
- Standard examinations should be reevaluated if they fall above specified numerical exposure guides.

This last guide addresses the overall system of equipment/material/operator performance by providing exposure guides (and I emphasize the word guides) for selected standard examinations that identify exposures that may be higher than necessary. This guide was based on a recognition that although each x-ray is evaluated for diagnostic quality when it is read, the exposure required to obtain it is rarely, if ever, evaluated. The thrust of the guide is the need to evaluate each system to determine if exposures are as low as reasonably achievable without loss of diagnostic information. Exceeding the exposure guides indicates that the system should be examined to reduce exposure; achievable exposures can generally be well below the guides and we believe they should be kept there whenever practicable.

Dental Radiography

Although most of the guides address both medical and dental radiography, certain of them are applicable to dental radiography specifically:

- Prescription of dental x-rays should be made only by licensable dentists on the basis of clinical evaluation.
- Performance of full mouth and routine x-rays should not be a routine part of preventive dental care.
- Dental technique should use long collimators with paralleling technique and with the x-ray field kept as near the image receptor size as practicable.

In approving these recommendations, the President directed the EPA Administrator and the Assistant Secretary for Health to carry out programs to interpret and clarify them as necessary. To this end, we have formed a Subcommittee of the Interagency Working Group on implementation of the guidance. This Subcommittee is chaired by the Bureau of Radiological Health in HEW. We are also planning to make an annual report to the President on the status of implementation of the guides.

There are several areas where implementation of the guidance could be assisted by development of more detailed or clarifying guidelines:

- Guidelines for use of appropriate shielding or collimation should be formulated for examinations where reduced exposure of reproductive organs or the fetus can be achieved.
- Exposure guides for some additional common examinations, such as mammography and panoramic dental examinations.
- Guidelines for quality assurance in specific areas are needed; these could include automatic film processors as well as other equipment and procedures in radiology departments.
- A benefit/cost assessment methodology should be developed for the evaluation of current and future x-ray screening programs.

It is expected that HEW will take a leading role through our Memorandum of Understanding in undertaking these activities; to date they already have in progress programs in the first three of these areas.

There has been some question concerning the extent to which this guidance applies to activities of Federal agencies other than direct health care delivery. The guidance was developed by Federal personnel who gave primary consideration to the proper conduct of radiation protection in Federal health care facilities, and it is applicable without additional consideration to such facilities. Application to other programs, such as research grants, contracts, and federally-funded public health programs is to a large degree a matter for the determination of each Agency. As is the case with previous Federal guidance, "it is expected that each Federal agency will use it as a basis upon which to develop detailed standards to meet its particular requirements" (43 F.R. 4379). The guidance does not require that agencies proceed to regulate areas other than those it would normally already regulate under its statutory authorities, policies, and agency goals. However, if an agency decides it has reason to establish requirements for radiation protection in the conduct of its programs, then we would expect that this guidance to Federal agencies be satisfied. Such application should not impede the provision of necessary medical benefits nor the obtaining of useful research results. I believe it would not be reasonable for EPA to attempt to specify in detail the circumstances where the guidance should be applied. However, because the guidance enunciates basic radiation protection principles, we believe it is likely to be applicable to most uses of diagnostic x-rays in any health care facility.

There are other major areas involving the use of radiation in the healing arts where the need for Federal guidance should be carefully examined. These involve the diagnostic use of radiopharmaceuticals and radiation theraphy, including the radiation treatment of benign diseases. These are being reviewed by our staff. As we address these areas, we intend to make maximum use of expertise and programs of other agencies.

In summary, we believe that the new Federal radiation protection guidance for diagnostic x-rays will lead to demonstration of significant reductions in exposure to diagnostic x-rays. It is our hope that this will become an important milestone in radiation protection and that this Federal example will provide the impetus for improved protection in the public sector. Thank you. I will be glad to attempt to answer any questions you may have.

federal register

WEDNESDAY, FEBRUARY 1, 1978
PART V

THE NATIONAL ARCHIVES OF THE UNITED STATES
1934

THE PRESIDENT

RADIATION PROTECTION GUIDANCE TO FEDERAL AGENCIES FOR DIAGNOSTIC X RAYS

Approval of Recommendations

presidential documents

[3195-01]

Title 3—The President

Recommendations approved by the President January 26, 1978

Radiation Protection Guidance to Federal Agencies for Diagnostic X Rays

Recommendations 1 through 12 contained in the above[1] memorandum are approved for the guidance of Federal agencies; the Administrator and the Assistant Secretary for Health are directed to conduct programs, in accordance with their respective authorities and their Memorandum of Understanding (42 FR 5123), to interpret and clarify, as necessary, each of these recommendations in cooperation with affected Federal agencies; the Administrator is authorized to issue these interpretations and clarifications in the FEDERAL REGISTER; and this memorandum shall be published in the FEDERAL REGISTER.

Jimmy Carter

Recommendations have been developed and are hereby transmitted for the guidance of Federal agencies in providing radiation protection for patients in the application of diagnostic x rays.

Executive Order 10831 and Public Law 86-373 (42 U.S.C. 2021(h)) charge the Administrator of the Environmental Protection Agency (EPA) to ". . . advise the President with respect to radiation matters, directly or indirectly affecting health, including guidance for all Federal agencies in the formulation of radiation standards and in the establishment and execution of programs of cooperation with States." In addition, the Assistant Secretary for Health in the Department of Health, Education, and Welfare (HEW) has a variety of responsibilities under the Public Health Service Act (Sections 301, 310, 311, and 354-360(f)) and the Federal Food, Drug, and Cosmetic Act bearing on the setting of health care policy and the use of radiation in the healing arts. These responsibilities, which have been delegated to the Food and Drug Administration (FDA), include research and training concerning radiation hazards, the development and promulgation of recommendations for radiation users, advise to the States, information for the public, performance standards for electronic products that emit radiation, and regulations for the sale, distribution, and use of medical devices.

Because of the special responsibilities of HEW involving national health care policy, which Federal radiation guidance for diagnostic x rays may impact directly, the Administrator and the Assistant Secretary join in requesting your approval of these recommendations. In this regard, on January 18, 1977, the two Agencies entered into a Memorandum of Understanding (42 FR 5123), which provides for the future development, within each Agency's respective authorities, of radiation protection guidance and, when necessary, updating of such guidance for uses of radiation in the healing arts.

BACKGROUND

Information on the diagnostic use of x rays in medicine and potential controls that could be applied without compromising benefits have been reviewed, and scientists and professionals within and outside the Government have been consulted in developing these recommendations. In this regard, we have benefited from the effort begun by the National Academy of Sciences—National Research Council for the former Federal Radiation Council to evaluate, interpret, and advise with respect to new knowledge on radiation effects and sources of population exposure. The report of the NAS-NRC Committee on Biological Effects of Ionizing Radiation was issued in 1972. One of its significant findings was that "[m]edical diagnostic radiology accounts for at least 90% of the total man-made radiation dose to which the U.S. population is exposed." More importantly, the Committee recommended that "[m]edical radiation exposure can and should be reduced considerably by limiting its use to clinically indicated procedures utilizing efficient exposure techniques and optimal operation of radiation equipment."

It is widely recognized by medical practitioners, medical physicists, and other scientists concerned with radiation protection that exposure due to medical uses of ionizing radiation represents a significant and growing source of exposure for the U.S. population and is also one that can be reduced by good practice. The National Council on Radiation Protection and Measurements has concluded that whereas "... there can be no rational means ... to limit radiation exposure prescribed for patients for necessary and proper diagnostic or therapeutic purposes[,] ... steps can be taken to minimize unnecessary or medically unproductive radiation exposure. ... Advantage should be taken of any new technology or procedure that will significantly reduce unnecessary diagnostic or medical exposure, both in individual examinations and treatments, and in the adoption of group screening practices."

---

[1] In the original document Recommendations 1-12 preceded the statement of Presidential approval.

An Interagency Working Group on Medical Radiation was formed by the Administrator on July 5, 1974, to assist in developing proposed guidance for diagnostic x rays. The Interagency Working Group determined that it is desirable and possible to reduce exposure from the diagnostic use of x rays in Federal facilities by: (1) eliminating clinically unproductive examinations, (2) assuring the use of optimal technique when examinations are performed, and (3) requiring appropriate equipment to be used. As a result of this consensus a subcommittee on prescription was established to examine factors to eliminate clinically unproductive examinations. Another subcommittee on technique was formed to examine the second and to some extent the third subject area where it might not be regulated by FDA's x-ray equipment performance standards, which became effective August 1, 1974. The reports of these subcommittees were made available for comment (41 FR 10705 and 27998) prior to completion of the Interagency Working Group report.

Proposed recommendations based upon the report of the Interagency Working Group were published for public comment (42 FR 4884) on January 26, 1977. In addition, there has been extensive commentary and discussion between EPA and HEW, as well as formal review by Public Health Service and other affected Federal agencies. The comments received have been carefully considered and a complete record, including a response to comments, is available to the public from the Public Information Reference Unit, Room 2922, U.S. Environmental Protection Agency, 401 M Street SW, Washington, D.C. 20460.

These recommendations were developed and reviewed in accordance with standard EPA procedures. Development of new or revised recommendations will be carried out under the Memorandum of Understanding referred to above, which provides also, when applicable, for theuse of HEW procedures.

DISCUSSION

The most important factor in reducing radiation exposure is to avoid the prescription of clinically unproductive examinations. Appropriate prescription of x-ray examinations involves two major considerations: (1) the clinical decision to order a particular examination, and (2) the minimization of the number of radiographic views required in an examination. In particular, attention should be given to the qualifications of those who order examinations, the elimination of unproductive screening programs, and the use of appropriate clinical procedures to assure that unproductive views are not performed.

Although the largest savings in radiation exposure may be realized from avoiding the prescription of an unproductive x-ray examination, patient exposure can also be reduced by assuring that the examination is performed with good technique. The fundamental objective in performing an x-ray examination is to obtain optimum diagnostic information with minimum patient exposure. Achievement of this objective requires assurance that: (1) equipment is calibrated and properly functioning, (2) equipment is operated only by adequately qualified personnel, (3) the patient is appropriately prepared, and (4) technique factors that will minimize exposure are selected.

It has been demonstrated that the same technique factors used with different x-ray generators may produce widely varying patient exposures. Thus, the performance of x-ray equipment utilized for diagnostic x-ray procedures is an important factor in limiting patient and operator exposure. The Federal Diagnostic X-Ray Equipment Performance Standard (21 CFR Part 1020) requires that x-ray equipment manufactured after August 1, 1974, be certified by manufacturers to comply with radiation safety requirements issued by the FDA pursuant to the Radiation Control for Health and Safety Act of 1968 (PL 90–602). Utilization of medical and dental x-ray equipment that performs in accordance with the requirements of this performance standard by Federal health care facilities would provide a significant contribution to the minimization of patient exposure.

Without question the use of x rays in the healing arts provides large benefits to society through improved health care; thus, in developing guidance for radiation protection for diagnostic x rays it is essential to assure that benefits to patients from the use of medical and dental x rays are maintained. Medical personnel in both the Federal and the private sectors have been consulted and we are confident that these recommendations will neither interfere with the doctor-patient relationship nor impair the ability of Federal agencies to provide necessary radiologic services.

Appropriate follow-up and coordination with Federal agencies is also important to assure that these recommendations are implemented so as to maximize their effectiveness in reducing unnecessary radiation exposure, but at the same time to avoid any deleterious impact on the delivery of health care. The Memorandum of Understanding between EPA and HEW referred to above is designed to assure that the dual objectives of radiation protection and health care delivery are achieved in the implementation of this or any future radiation protection guidance applicable to the healing arts.

RECOMMENDATIONS

In view of the considerations presented above, the following recommendations are made for the guidance of Federal agencies in their conduct of radiation protection for diagnostic uses of x rays in the healing arts:

1. General radiographic or fluoroscopic examinations should be prescribed only by licensable Doctors of Medicine or Osteopathy or, for specified limited procedures, postgraduate physician trainees and qualified allied medical professionals under their direct supervision; specialized studies should be prescribed only by those physicians with expertise to evaluate examinations in the particular specialty. Exception for specified procedures may be made for dentists and podiatrists.

2. Prescription of x-ray studies should be for the purpose of obtaining diagnostic information, should be based on clinical evaluation of symptomatic patients, and should state the diagnostic objective and detail relevant medical history.

3. Routine or screening examinations, in which no prior clinical evaluation of the patient is made, should not be performed unless exception has been made for specified groups of people on

the basis of a careful consideration of the magnitude and medical benefit of the diagnostic yield, radiation risk, and economic and social factors. Examples of examinations that should not be routinely performed unless such exception is made are:

a. chest and lower back x-ray examinations in routine physical examinations or as a routine requirement for employment,

b. tuberculosis screening by chest radiography,

c. chest x rays for routine hospital admission of patients under age 20 or lateral chest x-rays for patients under age 40 unless a clinical indication of chest disease exists,

d. chest radiography in routine prenatal care, and

e. mammography examinations of women under age 50 who neither exhibit symptoms nor have a personal or strong family history of breast cancer.

4. Prescription of x-ray examinations of pregnant or possibly pregnant patients should assure that medical consideration has been given to possible fetal exposure and appropriate protective measures are applied.

5. The number, sequence, and types of standard views for an examination should be clinically-oriented and kept to a minimum. Diagnosticians should closely monitor the performance of x-ray examinations and, where practicable, direct examinations to obtain the diagnostic objectives stated by clinicians through appropriate deletion, substitution, or addition of prescribed views. Technique protocols for performing medical and dental x-ray examinations should detail the operational procedures for all standard radiographic projections, patient preparation requirements, use of technique charts, and image receptor specifications.

6. X-ray equipment used in Federal facilities should meet the Federal Diagnostic X-Ray Equipment Performance Standard, or as a minimum for equipment manufactured prior to August 1, 1974, the Suggested State Regulations for Control of Radiation (40 FR 29749). General purpose fluoroscopy units should provide image-intensification; fluoroscopy units for nonradiology specialty use should have electronic image-holding features unless such use is demonstrated to be impracticable for the clinical use involved. Photofluorographic x-ray equipment should not be used for chest radiography.

7. X-ray facilities should have quality assurance programs designed to produce radiographs that satisfy diagnostic requirements with minimal patient exposure; such programs should contain material and equipment specifications, equipment calibration and preventive maintenance requirements, quality control of image processing, and operational procedures to reduce retake and duplicate examinations.

8. Operation of medical or dental x-ray equipment should be by individuals who have demonstrated proficiency to produce diagnostic quality radiographs with the minimum of exposure required; such proficiency should be assessed through national performance-oriented evaluation procedures or by didactic training and practical experience identical to, equivalent to, or greater than training programs and examination requirements of recognized credentialing organizations.

9. Proper collimation should be used to restrict the x-ray beam as much as practicable to the clinical area of interest and within the dimensions of the image receptor; shielding should be used to further limit the exposure of the fetus and the gonads of patients with reproductive potential (21 CFR Part 1000.50) when such exclusion does not interfere with the examination being conducted.

10. Technique appropriate to the equipment and materials available should be used to maintain exposure as low as is reasonably achievable without loss of requisite diagnostic information; measures should be undertaken to evaluate and reduce, where practicable, exposures for routine nonspecialty examinations which exceed the following Entrance Skin Exposure Guides (ESEG):

Examination (Projection)	ESEG (milliroentgens)*
Chest (P/A)	30
Skull (Lateral)	300
Abdomen (A/P)	750
Cervical Spine (A/P)	250
Thoracic Spine (A/P)	900
Full Spine (A/P)	300
Lumbo-Sacral Spine (A/P)	1000
Retrograde Pyelogram (A/P)	900
Feet (D/P)	270
Dental (Bitewing or Periapical)	700

*Entrance skin exposure determined by the Nationwide Evaluation of X-Ray Trends program for a patient having the following body part/thickness: head/15 cm, neck/13 cm, thorax/23 cm, abdomen/23 cm, and foot/8 cm.

11. X-ray examinations for dental purposes should be prescribed only by licensable Doctors of Dental Surgery or Dental Medicine or properly supervised postgraduate dentists on the basis of prior clinical evaluation or pertinent history; neither a full-mouth series nor bitewing radiographs should be used as a routine screening tool in the absence of clinical evaluation in preventive dental care. Exception may be made for justifiable forensic purposes.

12. Open-ended shielded position-indicating devices should be used with the paralleling technique to perform routine intra-oral radiography and should restrict the x-ray beam to as near the size of the image receptor as practicable.

It is expected that each Federal agency will use these recommendations as a basis upon which to develop detailed standards tailored to meet its particular requirements. In order to assure appropriate implementation of these recommendations, the Administrator and the Assistant Secretary for Health will cooperate in carrying out their respective functions in accordance with the Memorandum of Understanding (42 FR 5123). The necessary coordination will be conducted to achieve an effective Federal program, including periodic interpretation and clarification of each of the recommendations as required to reflect new information and changing technology. By so doing, it is expected that an achievable and reasonable reduction in x-ray exposure will be accomplished commensurate with a continuation of the vital benefits realized by the utilization of this important technology.

If the foregoing recommendations are approved by you as guidance for Federal agencies in providing radiation protection for patients in the application of diagnostic x-rays, it is further recommended that this memorandum be published in the FEDERAL REGISTER.

DOUGLAS M. COSTLE,
Administrator,
Environmental Protection Agency.

JULIUS B. RICHMOND, M.D.,
Assistant Secretary for Health,
Department of Health, Education, and Welfare.

[FR Doc. 78-2776 Filed 1-27-78; 3:31 pm]

Mr. ROGERS. Dr. Carter.

Mr. CARTER. Mr. Chairman.

By and large I agree with your presentation. It presents the good work that you have done. I do find your regulations quite reasonable. Do you have funds to study ionizing radiation?

Dr. ROWE. Ionizing radiation is one of our major concerns. We have no direct research programs in ionizing radiation, but we have, of course, funded the BEIR committee to update their 1972 BEIR report. We expect that this report will be available this fall. We use their collective scientific judgment as a major input to our health impact assessment.

Mr. CARTER. Actually, I believe you were required by the 1976 directive to concentrate on nonionizing radiation; is that not correct?

Dr. ROWE. No, sir. I am not sure what you are referring to.

Mr. CARTER. Well, in the report of the Comptroller General, January 20, 1978, it states on page 26:

> An effective radiation control program requires a strong scientific research effort to eliminate many of the uncertainties associated with health effects on environmental processes. EPA is currently performing no scientific research at all on the effects of ionizing radiation.

Dr. ROWE. Yes, sir, that is correct. As I said, we do no research directly on ionizing radiation. We depend upon other agencies.

Mr. CARTER. I thought you said you did. Maybe I misunderstood.

Dr. ROWE. We undertake a research program on nonionizing radiation, yes, but at the present time we have no ongoing effort in ionizing radiation research.

Mr. CARTER. I see. ERDA is supposed to be in charge of research on ionizing radiation; is that correct?

Dr. ROWE. ERDA, now the Department of Energy, has most of the funds for this research. There are other agencies, involved, however, such as the National Cancer Institute.

Mr. CARTER. We know those, of course. I believe I misunderstood what you said awhile ago. Thank you.

Mr. ROGERS. I understand that HEW and the Bureau of Radiological Health were not helpful to you in bringing these guidelines out; is that right?

Dr. ROWE. If I may take a minute, Mr. Chairman, a bit of history might put this in perspective. When we were formed back in 1970, and when I came on board in 1972, we had an uphill battle. We were the new boy on the block and we had been given a lot of responsibilities. Nobody wanted to see us intrude in various ongoing activities. We tried to exercise our responsibility. Initially, we got into some real tussles with the Atomic Energy Commission, and the Joint Committee on Atomic Energy, which, as you are well aware, no longer exist. We really spent quite a bit of time on jurisdictional issues. But we finally came out with our Uranium Fuel Cycle Standards in January 1977. People saw what they were and what they were meant to do. They have become pretty well accepted. As a result there are no longer such jurisdictional issues with the Nuclear Regulatory Commission. Such issues get put to bed after awhile.

Mr. ROGERS. So now the cooperation is good? It was difficult at first?

Dr. Rowe. That is right.

Mr. Rogers. Are you having any resistance anywhere within the Federal Government?

Dr. Rowe. Oh, yes, we continually do.

In the second case we had the same kind of problem with HEW. They challenged our authority to get into the medical X-ray guidance area, we are not going——

Mr. Rogers. How long did they delay the guidelines?

Dr. Rowe. I think it probably added at least 1 year or 2 to what we were trying to do.

Mr. Rogers. It took you 4 years to get these issued?

Dr. Rowe. I think it probably took us twice as long because we had to fight these other kinds of battles.

Mr. Rogers. Do you say you are still having opposition?

Dr. Rowe. I think we are still having opposition in some places. We are in the process of developing occupational guides, to replace the ones from existing Federal guidance. We would like to have the full cooperation of OSHA and NIOSH in doing this.

Mr. Rogers. You are not getting it?

Dr. Rowe. We are getting some cooperation, but less than we would like.

Mr. Rogers. I would like staff to make an inquiry on that; we will look into this.

Dr. Rowe. When we established an interagency group on the occupational guidance, we invited both of those agencies to participate. They turned us down, and did not participate.

Mr. Rogers. They turned you down? We will follow that up. Now why was this?

Dr. Rowe. Again, I think it is a challenge to our jurisdiction.

Mr. Rogers. All right. Now, let me ask this: How do we get these guidelines implemented throughout the non-Federal sector?

Dr. Rowe. Well, Mr. Chairman, we have no authority in the non-Federal sector. We hope that having these guides in the Federal sector as examples of good practice, we can hold them up to the private sector and say: "You ought to at least try to do as well as this."

Mr. Rogers. This committee will go into that. I do have other questions I will ask you to answer for the record, and we are grateful to you for being here. Your testimony has been most helpful. If you could get the answers to the questions in the record as soon as possible, the committee would appreciate it.

Dr. Rowe. Be happy to.

Mr. Carter. What is your reaction to the suggestion that the Federal Radiation Council or a similar type of committee be reestablished to coordinate Federal radiation responsibilities?

Dr. Rowe. Mr. Carter, I think one of the reasons why that was abolished in 1970 is that it proved to be unwieldy. It proved to be what in my opinion was an organization that made it difficult for things happen, as opposed to making sure that they did happen. More of a——

Mr. Carter. We certainly don't need that.

Dr. Rowe. I agree.

Mr. CARTER. I just wanted to comment. On page 9, I think I am in agreement with all the guidelines you have there. I have been over them rather carefully. Thank you, Mr. Chairman.

Mr. ROGERS. Thank you so much.

The next witness is Dr. Richard J. Gowen, Ph. D., director, Division VI, Institute of Electrical & Electronics Engineers, Inc., and president and dean of the South Dakota School of Mining & Technology, Rapid City, S. Dak. He is appearing on behalf of the Institute of Electrical & Electronics Engineers, Inc.

We welcome you to the committee.

STATEMENT OF RICHARD J. GOWEN, PH. D., MEMBER, BOARD OF DIRECTORS, INSTITUTE OF ELECTRICAL & ELECTRONIC ENGINEERS, INC., ACCOMPANIED BY THOMAS SUTTLE (WASHINGTON OFFICE); AND JAMES HEVEZI, PH. D.

Dr. GOWEN. Thank you, sir.

Mr. ROGERS. Your statement will be made part of the record in full, and if you can highlight it for us, the committee would appreciate it.

Dr. GOWEN. Appearing with me today is Dr. James Hevezi who is a member of the faculty of South Dakota School of Mines and Technology and a radiation physicist and Mr. Tom Suttle, with the IEEE office in Washington, D.C.

We are very appreciative of the opportunity to be with you today. Sir, if I could, I should like to look at the summary that we have presented and try to highlight a few of the points. [See p. 1147.]

Mr. ROGERS. Certainly.

Dr. GOWEN. There are five points we would like to bring to your attention, if we may.

The first point I would like to address deals with the issue of the trend for regulation. The IEEE represents some 165,000 members. We are very much in support of the process of improving health care. We speak to you today from the point of technologists and people who are very anxious to develop the technology needed for health care. We have a long history of support of that type and would like to continue it and try to be of service.

One matter of concern to our members is that there appears to be a trend within the regulatory process of regulating technology as one means of controlling the excessive use of radiation. Our concern, sir, is not that we regulate excessive radiation; we support that. We clearly want to make sure regulations are effective in that regard. Our concern is that through the regulatory processes we tend to cause those people in the R. & D. development, development of new technology, to shy away from the technology markets, to move out of the development process. Our concern is that the very thing we are trying to achieve, that is, improved technology for health care delivery, is in fact discouraged and we see the opposite. Some regulations cause those people who develop the new advances, new improvements leading to lower radiation exposure, to put them efforts elswhere. There are many markets they can move to.

However, there is a very, active development within the new technology, and clearly continued development requires that the marketplace continue to be attractive. That is one of the concerns of our membership. I would like to bring the need for cost to benefit analysis in regulations to your attention and I will be happy to amplify this concern if you wish.

A second area of concern to our membership is the question of training and continued development. In particular we would like to recommend that a program be established to increase the competency of persons who use radiological equipment, stressing the potential dangers. We are concerned that it is estimated that over half of the operators of radiologic equipment in the United States have received no formal training. New advances in X-ray imaging require special expertise to use the equipment more efficiently and programs of continuing advanced training of medical professionals are essential.

In a study to determine the cost comparisons between the use of X-ray images produced by conventional means and computed tomographic means, a report by the A. D. Little Corp. referenced in the prepared statement, shows that with the ready availability of computed tomographic scanners, the number of X-rays produced by conventional means shows only a 5.5-percent reduction by the year 1980. Clearly the benefit will come from increased ability for diagnosis, and in reality a reduction in the need for exploratory surgery. This will result in considerable savings in comfort, morbidity, and dollar cost to our patients. Yet the point is well made that there will remain need for conventional X-ray technology. Such a need is going to be with us far into the future. We have a tremendous investment in conventional technology. Within that conventional technology there is clearly a need for looking at how we can better use the technology for lessening X-ray exposures.

In engineering we look at the procedure of deciding amongst alternatives as a tradeoff. We try to take a look at the pros and cons, on the one hand evaluating additional regulation, on the other hand developing a system to bring about the desired improvement at minimal cost. It appears one of the major concerns that should be looked at is supporting ways of developing greater competence and expertise within the very people who use X-rays? Let me be clear: I am not speaking in terms of the radiologists who are well-trained and knowlegable in the use of X-rays. I am directing our concerns to the people who use the equipment—the technicians and non-radiology trained physicians. Many are very competent and well-trained, but unfortunately many are not.

There is a tendency to try to develop, and design equipment to take care of that lack of expertise in the individuals. This approach is quite expensive and perhaps not cost-effective. Our suggestion is that you consider, in the tradeoff sense, looking at what the real benefit might be if we could provide better entry education and encourage continuing education for users of X-ray equipment.

We look to Federal support, for such education. There are many interesting effects of such a program. One would be the consideration of the delivering of such education. Consideration should be given to educational programs as presented through the Public Broadcasting System. Clearly there is a need for large numbers of people to be brought up to a level of proficiency. In education today we have that in the Public Broadcasting System the publication hours during the day are used to support primary and secondary education. We find that 27 percent of the adults know many of the characters that occur on those daytime educational shows for schoolchildren. I bring that point to your attention really as one of the concerns that we have is that the general public is not aware of the dangers associated with radiation, with X-rays. We develop such an educational program, there is an important secondary consideration in choosing a delivery means such as educational television, which will lead to considerable education of the general public. We suggest action to create an education program now as a joint effort between the Government, the various professional groups and societies, and those who are involved themselves. Our suggestion, sir, is that this might be an area that a dollar would be well spent.

We also would like to propose and suggest for your consideration and assistance that a program be established to provide continuing education to health care professionals in the optimal use of new radiologic equipment. The program objectives should be to minimize the amount of exposure to ionizing radiation, to obtain greater information from each exposure, and to better utilize these costly resources of highly trained individuals and technologically advanced equipment.

Continuing education is essential for radiologists and physicians who use the resultant images that come from such high-technology equipment available today. Such education should include the extension of the practitioners' knowledge of the benefit-to-cost tradeoff for the patient with each additional X-ray exposure. Support should be given to programs to develop educational packages to help acquaint radiologists with the potentials for greater use of the computed tomographic scanner.

Such training programs are especially important as the radiologist moves from conventional techniques to those available with the computed tomographic scanners. Now is the time to provide for the development of educational packages for the transition from both conventional X-ray equipment and present scanners to realtime scanning techniques. Realtime scanning is around the corner. It is the new technology development. It has the effect, sir, of not taking an X-ray and seeing it later but doing it in much the same way as the fluoroscope. It is very high-priced technology. When one looks at the price the health-care system it is clear that investment will be almost the same magnitude as present CT scanning. There needs to be planning for that now. I am speaking to you not only that there are dangers with radiation, but that the multiple delivery paths increase the dangers of excessive radiation.

Another point I would like to address, sir, is that we consider those people who are involved in using technology, particularly the technicians, and encourage the adoption of voluntary certification. In the past there has been discussion for having licensure for technicians, and there are approximately 150,000 of them in the United States, and that would represent a tremendous impact upon the health-care professions.

Rather than licensure we would very much like to support the concept of certification, in particular the concept of certification that would tie with it a benefit to the hospital that would encourage their people to pursue certification.

This brings us to the concept of incentives. We would like very much to ask that exploration be brought forward to try to determine how we might bring better incentives into the technology and health-care community interface. I speak to you today as a medical researcher, a person who is involved very much within the medical community and a person who is involved with technology. One of the concerns that we see in the present trend of limiting costs by regulation. Clearly as taxpayers and as patients we are very anxious to limit costs. There needs to be careful balance between the problem of supporting expensive technology development and increasing costs. There needs to be opportunity for continued growth within medical practice, which translates we need some better technologies.

We hear a lot of discussion about caps, about lids, putting on limits, and additional regulations that in essence would restain growth.

We respectively suggest that the committee call for a panel of health care providers and managers, bankers, third-party payees, manufacturers, and engineers to be convened to develop incentives for the continued development of advanced technological equipment. This panel should also evaluate incentives for cost containment with the introduction of new advances in imagery technology.

We would also like to ask you to consider methods by which research could be supported and encouraged for the development of new technologies that will provide medical diagnostic images at reduced exposure to radiation, such as ultrasound. It is a technology which has a lot of attraction, but it has a lot of problems. It is far from the level of development that we see with CT scanners. But there are many advantages with ultrasound. So the area of continued development is of great concern to us. We should like to help in any way that we can to assist in the development of appropriate review panels and regulations to see that continued development will occur.

The next area I would like to touch, sir, is a little bit sensitive in the sense what we suggest that a close look be made at the question of how many X-rays are really necessary. Our concern is whether there are needless X-rays being taken. Our approach to the problem is to suggest that we examine traditional modalities of practice we find that the present use of X-rays within the hospital system are generally used in a system in which a physician, the primary care provider, determines that there is a need for a diagnosis and requests there be an X-ray taken. In the process of that X-ray being taken we generally follow an all-or-nothing approach in which you take all of the views regardless of the potential diagnosis.

From a systems standpoint and looking at the problems involved, that tends to appear like there could be other optimizations. In our statement, we suggest, sir, that consideration be given to changing the procedures used in making an X-ray diagnosis. With the availability of more trained operators, encouragement be given to radiologists to develop imaging techniques and procedures to minimize patient exposure to radiation. We also would like to suggest that we explore developing ways to provide protection to the medical practitioners from the threat of malpractice which will take the place of multiple X-ray exposures to provide documentation of medical devices.

In conclusion, thank you very much for the chance to be with you today and the opportunity to explore how we in the engineering and science professions can be of service to you and your committee.

[Testimony resumes on p. 1174.]

[Dr. Gowen's prepared statement and attachments follow:]

A STATEMENT ON THE DEVELOPMENT OF TECHNOLOGY TO PRODUCE DIAGNOSTIC MEDICAL IMAGES WITH IONIZING RADIATION

FOR PRESENTATION TO THE
SUBCOMMITTEE ON HEALTH AND THE ENVIRONMENT
OF THE
COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE

BY
RICHARD J. GOWEN, PH. D.
MEMBER OF THE BOARD OF DIRECTORS,
INSTITUTE OF ELECTRICAL AND ELECTRONIC ENGINEERS, INC.
AND
VICE PRESIDENT AND DEAN OF ENGINEERING
SOUTH DAKOTA SCHOOL OF MINES AND TECHNOLOGY
JULY 15, 1978

SUMMARY

The Institute of Electrical and Electronic Engineers, the largest scientific and technical society in the world, with a membership of engineers and scientists who have had a long and successful history of interaction with medical practitioners in the development of advanced technology in support of the delivery of health care, whose members are deeply concerned with developments affecting the use of ionizing radiation in medical diagnostic imaging, recommends the following actions:

1. The trend toward the use of greater federal regulations to limit advances in technology which supports improved health care be stopped.

   In an effort to control the misuse of technological advances, such as diagnostic x-ray machines or the computed tomographic scanner, federal regulations discourage the development of new technology.

   a) A panel of engineers and scientists be formed to determine the trade offs between the benefits and costs of all regulations affecting equipment and medical devices, particularly those that use radiation in the diagnosis of medical disorders and disease.

   b) An indepth evaluation be made of the organization and procedures of health care delivery to determine how to optimally control the misuse of health related technological advances.

2. A program be established to increase the competency of persons who use radiological equipment stressing the potential dangers.

   It is estimated that over half of the operators of radiologic equipment in the United States have received no formal training. New advances in x-ray imaging require special expertise to use the equipment more efficiently and programs of continuing advanced training of medical professionals are essential.

   a) A joint educational program be developed with professional organizations and government to develop materials and presentation methods to train operators of radiologic equipment in techniques which will minimize exposure to x-ray radiation.

   b) A program be established to provide continuing education to health care professionals in the optimal use of new radiologic equipment. The program objectives should be to minimize the amount of exposure to ionizing radiation, to obtain greater information from each exposure, and to better utilize these costly resources of highly trained individuals and technologically advanced equipment.

   c) A program of voluntary certification of radiological operators be developed with incentives provided to hospitals and health care providers who participate in the program.

3. Incentives be developed to encourage the continued growth of technology to improve radiological imaging at both reduced radiation exposure and cost.

   Rapid changes in technology lead to early obsolescence of equipment before development costs can be recovered in the usual manner and the resulting high cost of equipment contributes to increases in the cost of patient care. Regulations to contain costs discourage the development of new technology for improved patient care. Incentives-to manufacturers, hospitals, and care providers could limit the inflation of health care costs and still provide for needed improvements in equipment for better patient care with less exposure to radiation at lower costs.

   a) A panel of health care providers and managers, bankers, third party payees, manufacturers, and engineers be convened to develop incentives for the continued development of advanced technological equipment. This panel should also evaluate incentives for cost containment with the introduction of new advances in imagery technology.

   b) Research be supported and encouraged to develop new technologies that will provide medical diagnostic images at reduced exposure to radiation.

4. An evaluation of radiologic procedures and techniques be made to minimize the amount of exposure to ionizing radiation required to arrive at a diagnosis.

   Present procedures are optimized to provide all images that could be required for a difficult diagnosis at the lowest cost to the provider rather than minimizing the radiation exposure to the patient.

   a) With the availability of trained operators, encourage radiologists to develop imaging techniques and procedures to minimize patient exposure to radiation.

   b) Develop ways to provide protection to the medical practitioner from the threat of malpractice which will take the place of multiple x-ray exposures to provide documentation of medical devices.

5. Encourage the development of alternative diagnostic imaging techniques.

   Technologies are evolving to produce diagnostic images using ultrasound and thermographic techniques. While useful in many types of diagnosis today, considerable research and development is necessary before the technology will be advanced to the point of significantly replacing ionizing radiation as a diagnostic imaging technique. Research and development funds are essential.

The IEEE offers the professional services of its many members to assist in the solution of problems concerning the use of ionizing radiation to provide medical diagnostic images.

INTRODUCTION

Mr. Chairman, and members of the Committee, on behalf of the Institute of Electrical and Electronics Engineers, usually referred to as the IEEE, I wish to express my appreciation for the opportunity to present this statement expressing our concerns. I speak to you today as a member of the Board of Directors of the IEEE which represents those members of our Institute with direct interest in the delivery of health care and medically related research; development and manufacture.

The IEEE is a professional society of engineers and scientists with over 165,000 members in the United States alone. This organization has as its origin the incorporation in New York State in 1884 of the American Institute of Electrical Engineers, which merged with the Institute of Radio Engineers in 1961 to form the Institute of Electrical and Electronics Engineers, the IEEE. In its 96 years of existence the membership has grown from 46 to over 185,000, and its scope has continuously expanded to meet the many needs of our profession as we serve society during this exciting and challenging time of rapidly changing technology. The IEEE is the worlds largest scientific and technical society and is recognized as a major institution in the field of engineering on both the domestic and the international scene. Its members cover the entire spectrum of associated interests, including teaching, research, government and industry, private individuals, small business, and mammoth multinational enterprises.

The IEEE has had a long and exciting history of involvement in the application of technology to the solution of problems in health care. The technical interests of the members of the Institute are focused through 32 societies, groups and councils (1). These technical entities publish transactions of new research and developments, hold conferences, and in general, function much as a separate society would, yet they are all under the umbrella of the Institute. Their interests cover the entire spectrum of modern electrical science and technology ranging from computers to ultrasonics to electrical power to engineering in medicine and biology and many other fields. Many of these Societies have particular expertise appropriate to the interests of this committee and I have attempted to coordinate their contributions in this statement. The IEEE has played a major role in the development and manufacture of equipment through its extensive efforts to develop and maintain voluntary standards in the many areas of electroscience technology. This standard program is a vital part of providing safe and effective technology for the delivery of health care.

In particular I would like to note the IEEE Committee on Man and Radiation (COMAR) which is composed of eminent scientists and engineers with special expertise in the field of non-ionizing radiation. This committee has provided information in service to the congress in the past and, as with the rest of the Institute, stands ready to provide its assistance at any time.

Mr. Chairman, it may be helpful to you and the committee to know that I am an electrical engineer by training who has specialized in the solution of problems in medical research and health care delivery. I am a registered professional engineer and am certified in clinical engineering. My experience includes the direction of space medical research for NASA; systems analysis consultation on the productivity of the military health care system; and educational program development. I am an elected Director of the IEEE, having previously served as the President of the Engineering in Medicine and Biology Society of the IEEE and the Vice President and Dean of Engineering of the South Dakota School of Mines and Technology.

There is growing concern within our membership that regulatory emphasis to protect the public is becoming increasingly misdirected toward regulating the development of technology (2). As citizens of this country, we are deeply concerned that the true good of the public be served. Advances in technology have brought tremendous new opportunities for improvement in the delivery of health care. We have all come to expect quality health care at a reasonable price. Today's technological advances bring that dream of excellence in health care delivery into the reach of every citizen of these great United States. The challenge of today is to make that dream of excellence in health care a reality using the available resources. As a nation we have already improved our quality of life in so many areas that we have good reason to question why we should continue to have such grave concerns about the uses of ionizing radiation in the delivery of quality health care.

The IEEE, through its volunteer membership, using the many avenues of technical exchanges between engineers and scientists, has had a long association with the development of the techoology used in the delivery of health care. As engineers, our members have sought to apply the newest scientific developments to create the best equipment to further the practice of medicine (3), we are concerned that we shall be able to continue to provide the optimal development of technology at a reasonable cost to aid the practitioner in making the diagnoses so vital to our continued well being.

HISTORICAL PERSPECTIVES

Since the discovery of the x-ray by Conrad Roentgen in 1895, a major application of this technology has been the production of medical x-ray images. The ability to visualize parts of the human body without surgical penetration has become a hallmark of modern medical practice. With the first medical x-ray produced in this country in 1896, a new era in medical diagnosis was born. An era in which medical practitioners could now peer into the human body and discover the basis for numerous pathologic conditions heretofore undetectable.

The era brought together the elements of the technological community and the medical community in a marriage that produced truly remarkable achievements in health care delivery. It has culminated in the invention and immediate introduction to the medical diagnostic community in 1972 of perhaps the crowning achievement of this marriage: the computed tomography scanner (4). Table 1 as found on the following page shows some of the major technological achievements influencing the development of diagnostic x-ray images (5,6) and Appendix I presents an encapsulated description of the CT method of operation for your information.

Images produced by this sophisticated equipment enable the diagnostician to obtain virtually "anatomical atlas" quality visualization of the internal body structures not possible previously. Indeed, it has become the mode of choice in diagnostic examinations of the brain, and is rapidly becoming the diagnostic technique of choice in several other organ systems of the body.

TABLE 1

DEVELOPMENTS IN MODERN RADIOLOGY

DATE	EVENT
1887	Hertz produces electromagnetic waves
1895	First alternating current power system installed at Niagra Falls
1895	Marconi transmitts wireless telegraphy 1 Km
1895	Roentgen discovers x-rays
1896	First medical applications of x-rays in diagnosis and therapy
1897	J. J. Tompson discovers the electron
1900	Roentgen Society formed, first American radiology organization founded, in 1902 became American Roentgen Ray Society
1901	Roentgen receives first Nobel Prize in physics
1904	Fleming invents the vacuum diode
1905	Einstein introduces theory of relativity
1913	Bohr atom conceptualized, central nucleus with planetary electrons
1913	Coolege hot w-filament x-ray tube developed
1916-18	Cellulose nitrate photographic film base developed and adopted
1919-21	Investigators demonstrate use of soluble iodine compounds as x-ray contrast media
1921	Potter-Bucky grid is introduced
1922	Compton describes the scattering of x-rays
1929	Forssmann demonstrates cardiac catheterization
1930	Tomographic devices demonstrated by several investigators
1937	International Committee on X-Ray and Radium Protection officially defines the Roentgen as the unit of x-ray intensity
1942	Morgan exhibits an electronic phototiming device
1945	Public awareness of radiation health hazards based on atomic bomb casualties
1946	Bell Telephone laboratories develop light amplifier tube
1948	Coltman (at Westinghouse) develops the first fluoroscopic image intensifier
1953	The rad is officially adopted as the unit of absorbed dose. The Roentgen is defined as a unit of exposure in air.
1956	Xeroradiography is demonstrated
1968	Radiation Control for Health and Safety Act (Public Law 90-602) passed by Congress
1972	Hounsfield working at EMI introduces the CAT scanner to diagnostic medicine
1976	Several x-ray equipment manufacturers introduce whole body CAT scanners with sub-10 second scan times

As with many technological achievements, the development of x-rays has raised serious questions concerning their effect on the very people served. Our appreciation of the harmful effects of radiation have brought us from the time of such popular use of x-ray machines to visualize how well our toes fit within our new shoes to the deliberation of such grave questions as the existence of a threshold level beyond which the use of x-rays for the pre-clinical diagnosis of breast cancer would be judged unacceptable for screening.

The development of x-ray equipment has been a classic story of applied technology to improve the medical image while reducing the radiation exposure to the patient. Developments in electronics have rapidly been applied to diagnostic x-ray equipment. One such example is the use of the image intensifying tube to produce flouroscopic images with television recording and display. In 1946 the Bell Telephone Laboratories made available image intensifier electronics tubes which were applied by Coltman in 1948 to produce the x-ray image intensifier. It now became possible to visualize dynamically, internal organs using remarkably reduced levels of x-ray radiation.

This trend toward improved images with reductions in the level of radiation exposure required has continued to the development of the computed tomographic scanner of today. However, there is an apparent limit to this approach. The fundamental principle of imagery with x-rays is the determination of the differential absorption of the x-ray beam by body tissue. Bone absorbs x-rays differently than soft tissue. More dense tissue matter, such as some carcinomas, absorb x-rays to a greater extent than do surrounding tissues. Thus, an x-ray image is in fact a representation of the differing rates of absorption of x-rays by the various tissues of the body. The quality of an image is improved as the distinctions in absorption become sharper. Additionally, the desire to reduce the exposure of the patient to radiation leads to x-ray beams with as low a level of radiation possible to just enable the radiation detector, either film or electronic, to distinguish between various tissue systems. There is a practical limit beyond which the further reduction of the intensity of the x-ray beam will only lead to the loss of detail in the desired x-ray image. This limit exists because of the inherent characteristics required to produce an x-ray related image signal that is significantly greater than the random density images forming the background against which the medical image must be visualized. Continued research in the development of new more efficient sensors is essential to facilitate further reductions in the exposure to the patient while preserving the requisite image fidelity.

It is this drive for improved images at lowered levels of patient radiation that has led to the development of the computed tomographic scanner. In this procedure, applications of the same computer enhancement techniques used to send back pictures from distant planets has been used to enhance the x-ray image presented to the practitioner. Here is another example of the application of advanced technology, in this case the technology of computer signal enhancement, to further reduce the x-ray radiation required to produce a greatly improved image.

If we only focus our attention on the radiation exposure to the patient who is in need of a skull series of x-rays to help diagnose a suspected tumor of the brain, we shall see that the x-ray image developed using the computed tomograph requires about the same level of exposure to radiation compared to that of a standard skull series using previously available x-ray techniques (7). But of greater importance is that the x-ray images produced by the computed tomographic scanner present significantly improved information to the practitioner who must prescribe the course of medical intervention most suitable for that patient's condition. It is this improvement in organ imaging that has led to the rapid acceptance of such expensive machines. Computed tomography promises to replace significant percentages of the neurological procedures that would be performed in the absence of computed tomography (9), 20% for cerebral angiography, 70% for pneumoencephalography, 45% for radionuclide brain scans, 5% for skull x-rays, and 50% for exploratory brain surgery. These new technological developments are costly but they bring the potential for higher quality health care to all our citizens. In the right hands, such powerful devices can produce information that is invaluable. Yet, there seems to be an underlying suspicion that in the wrong hands these new marvels will lead to only needless costs and duplication. Unfortunately, we seem to lose all too easily , sight of the fact that technology has produced a tool that can be invaluable if properly used. It has become popular to charge that technology is responsible for driving up the cost of health care delivery. Our challenge today is to bring these tremendous improvements in diagnostic imagery to the greatest numbers of people at a cost they can afford, not by limiting the development of technology, but by limiting needless examinations and wasteful duplication.

REGULATION OF TECHNOLOGY

In an attempt to regulate needless radiation exposure, the 1974 Regulations promulgated through HEW mandated safeguards to be added to all radiographic equipment manufactured after 1974. The thrust of these regulations was to ensure that the exposure to the patient was minimized by directing that greater emphasis be placed on the automatic protection of the patient through technological means. Much of the x-ray technique adjustment has been taken out of the hands of the technologist. Procedures to automatically limit the exposure field of the x-ray beam to the image receptor size chosen have aided in minimizing the exposure of the patient. Further, basic automatic control of the amount of ionization penetrating the patient to the film image surface promises to reduce the exposure even more.

However, one must question whether these regulations affected the optimal method to achieve the desired reduction in x-ray exposure. Clearly, there is an additional cost with the addition of this new automatic control equipment on each x-ray machine. Our challenge is to find ways to bring quality health care as described in testimony presented in 1977 to the Committee on Commerce, Science and Transportation of the United States Senate by Dr. Morgan of the American College of Radiation (ACR) where in he noted that the impact of the FDA 1974 performance standards for diagnostic equipment "to provide for positive beam limitation has added approximately $1,200 to $6,000 to the cost of each stationary, general purpose diagnostic x-ray unit" (about 50% of all x-ray systems are of these types costing from $20,000 to $100,000) (9). The statement of ACR continues to point out that while these beam limiting devices have proven to be complex and difficult to operate and maintain, other requirements, "such as the one for fidelity of beam production within 2 percent of setting, have also added to cost, while delivering a superior piece of equipment".

Where regulatory activity results in a safer, more reliable piece of equipment that adds to the diagnostic process, the added costs of regulatory activity can be justified. However, such costs must ultimately be passed on to the patient.

In principle, the costs of regulatory activity does not stop with the price of regulatory equipment or special devices. The patient is faced with an additional cost, often beyond a dollar value, resulting from the discouragement of the continued development of new technological devices which could provide improved care. As an example, the Medical Device Act of 1976 provides for the close control of the manufacture of medical devices, which on the surface is a lauditory goal. In the January 1975 issue of Spectrum, the IEEE Membership magazine, the effect of these regulations to limit the development of new medical technology is discussed (2). The article shows how the manufacturer of a special cutheter for cardiac procedures was unable to continue production due to the excessive costs to meet the FDA regulations when balanced against the limited market for the product. The market was established to be approximately $15,000 per year and the cost of compliance at $200,000. Thus, while insuring that the patient would be protected, the regulations had the ultimate effect of removing the product from the market place and hence denying those few patients who required the catheter the excellence in care that was technologically available.

An additional concern of our members is the strangulation effect that excessive or poorly directed regulations have on the development of new technology. It is true that if we stop the development of new advances in health care technology, we would then have little to attract the health care professionals who seek to bring the best care available to their patients. Such action would clearly limit the growth of the cost of health care.

An example of this concern for the discouragement of technological change is found in the continued development of the computed tomographic scanner. Present scanners are estimated to cost over $325,000 per year (5 year depreciation and operating costs) per installation (8). Yet, in 1977 the first of the next generation of realtime scanner was announced (10). The development of such a realtime scanner has the potential for an impact on the practice of medicine greater than that of our present scanners. The ability to "see" an image of an organ as it is actually functioning, and to be able to correlate such activity with other physiological measures present a whole new vista of mecial practice. Clearly, such machines will be in demand to both augment and replace todays still unpaid static scanners.

We must avoid the discouragement of such a potentially significant medical instrument. Potentially significant because only the most gifted are able to visualize the unlimited applications and possible new procedures that could drastically alter the practice of internal medicine. We must meet the challenge and realize that the solution is not to limit the development of technology, but to examine the organization of the system of health care delivery. Such is not an easy task. It is far simpler to limit access to some piece of equipment than to cope with the need for fundamental changes in the organization and procedures of health care delivery.

I urge this committee to recommend the adoption of a cautious posture, a questioning posture, an evaluative posture concerning the promulgation of additional regulations that could stiffle the development of new equipment and procedures providing better health care delivery. I encourage the committee to call for a careful evaluation of the impact of the 1974 and 1976 diagnostic radiation device and medical device regulations. Not only the impact in dollars, but the real impact in delivering the most efficacious care to the patient. Mr. Chairman, may I ask you to call for the appointment of a "blue ribbon" panel of engineers and medical scientists to evaluate the costs and benefits of all proposed and existing health device regulations. There is an urgent need for an independent panel to make what we in engineering call, a "trade-off" study, which is an indepth evaluation of the impact of proposed changes. The use of such a "trade-off" or sensitivity study is simply a systematic means of exploring and evaluating all realistic approaches to the solution of a particular problem. We use such analyses whenever it is essential to optimize the impact of possible decisions. Our members support the need to optimize our limited resources in combination with a need to reduce the radiation exposure to the patient. Such a "blue ribbon" panel can serve a vital purpose in the integration and evaluation of the many comments, suggestions, and evidence presented concerning the impact of proposed regulation in the application of technology to better health care. As potential patients, we call for the true optimization of the entire health care delivery system, not simply the psuedo optimization of technology. Now is the time to evaluate, and as necessary recommend changes, in the roles and effectiveness of the individuals charged with health care delivery.

EDUCATION AND TRAINING

The potential exists for the production of an x-ray machine which requires little interaction from the operator. Such is the case with todays computed tomographic scanner. This is a "smart" machine that all but ensures that the patient will receive the minimum exposure consistent with the production of a high quality image. However, while the use of computed tomographic images is growing, it still represents a small percentage of the total use of diagnostic x-rays.

In a study to determine the cost comparisons betwen the use of x-ray images produced by conventional means and computed tomographic means, a report by the A.D. Little Corporation shows that with the ready availability of computed tomographic scanners, the numbers of x-rays produced by conventional means shows only a 5.5 percentage reduction by the year 1980 (8). This study emphasizes that the real benefit of increased use of computed tomography is the reduction in the need for exploratory surgery, with considerable savings in comfort, morbidity, and dollar cost to the patient. Yet, the point is well made that the need for conventional x-ray technology will remain with us for the forseeable future. Let us evaluate some of the needs to improve the operation of today's conventional x-ray systems.

The number of conventional x-ray systems in use for diagnostic x-ray imagery has been estimated at over 100,000 units. These systems represent a large capital investment estimated in excess of one billion dollars. These systems are by and large already paid for and represent a minimal expense to the user. The Little study shows that a brain scan with a computed tomographic scanner will have an average unit cost of $250.00. A similar procedure using conventional means will cost $36.00. The largest elements in the cost of a conventional x-ray are the salary of the radiation technologist and the fee to the radiologist for reading the x-ray film. These machines must be manually adjusted for the correct technique and require that the operator be highly trained.

We are concerned that approximately half of the 150,000 operators of radiologic equipment in the United States have received appropriate formal training (11). This situation is of further concern because, as stated by Mr. C. Hardin, representing the Conference of Radiation Control Program Directors before the Senate Committee on Commerce, Science, and Transportation in 1977 (11),

> ". . . I would like to express another concern of the states which has also been expressed at the federal level. Specifically, as reported in the Bureau of Radiological Health staff report entitled "Diagnostic Medical X-Ray Technologists: The Issue of Qualifications," dated January 19, 1975: "With the exception of 13,000 radiologists, who are expert in the use of radiation for diagnostic and therapeutic purposes, physicians are generally not trained in the principles and practices of radiation protection, and what radiologic training the non-radiologists physician does receive, either in medical school courses or during the clerkship or internship periods, is almost entirely concerned with part of physicians' training, and this is particularly significant in view of the fact that the performance of the examination is largely delegated by physicians to more than 100,000 x-ray machine operators, many of whom do not possess formal credentials certifying their competence. The situation in many instances, then, is that of a supervisor untrained in radiation protection directing an equally untrained employee.""

In the tradeoff or sensitivity study of the x-ray diagnostic system, it is clear that there is a high benefit to cost payoff (including the cost of unnecessary radiation exposure) if additional training and continued education is developed for the operators of diagnostic x-ray systems.

A major question is: Who should provide such training? We recommend that a joint effort be initiated, with industry, the hospitals, the professional societies, and the government joining forces to develop a training program reaching all corners of our country. The IEEE through its many member technical societies stands ready to assist in such a program. Ideally the implementation of such a health training service could be accomplished under the aegis of the state health agencies. The federal government, in cooperation with the third party payees, could provide an incentive for those hospitals, clinics, and radiological services that avail themselves of such training. The professional societies coulf assist in the preparation and continued updating of the materials. Potential delivery techniques range from the use of educational television, with the resultant secondary effect of an informed public (over 27 percent of the adult population is familiar with the characters used in daytime school aged educational television), to home study audio-visual materials, conferences, and workshops.

In addition to providing an incentive system through payments to the care providers for encouraging these operators to participate in such training, a program of certification and recertification of competency is essential. While it is clear that the Federal government could legislate that such certification is required of all persons who operate radiological devices, it is equally clear that such legislative action would not receive enthusiastic support from radiation technologists and hospitals involved. Perhaps a more acceptable approach would be to provide for voluntary certification rather than mandatory licensing. Such certification could serve as a basis of fee authorization and payment to the health care providers.

The IEEE is dedicated to excellence in engineering and science and supports programs to recognize and reward proven competency. This is particularly the case in the practice of engineering that has a direct impact on the public, such as in the development of health care technology. It is the policy of the IEEE to encourage the licensure and registration of engineers as professional engineers when they are responsibly involved in products that have an impact on the public (12). I ask that this committee join in supporting our goal that at least a minimal level of competency be assured in the design, assembly, and evaluation of x-ray equipment through the proper employment of professional engineers for positions requiring the exercise of engineering approval of equipment that will have a direct interface with patients such as x-ray equipment. Those persons who wish to demonstrate their high levels of competency in the application of engineering in the direct support of patient care delivery, can be certified as slinical engineers by meeting the exacting requirements of the American Board of Clinical Engineering. These clinical engineers are becoming available in increasing numbers in hospitals and industry today to aid in the solution of such complex problems as the management of technological developments within the health care delivery system.

In addition to those who build and those who operate x-ray equipment, continuing education is most essential for the radiologists and physicians who use the resultant images. Such education should include the extension of the practitioners knowledge of the benefit to cost trade off for the patient with each additional x-ray exposure. Support should be given to programs to develop educational packages to help acquaint radiologists with the potentials for greater use of the computed tomographic scanner.

Such training programs are especially important as the radiologist moves from conventional techniques to those available with the computed tomographic scanners. Now is the time to provide for the development of educational packages for the transition from both conventional x-ray equipment and present scanners to realtime scanning techniques. The computed tomographic impact to date has represented a completed revolution in the procedures of how diagnostic imaging procedures are performed. The availability of realtime computed tomography promises an even greater revolution with even more efficient uses of x-rays to provide better diagnoses with dynamic studies.

The IEEE supports and recommends passage of the Senate Bill 5.2388 sponsored by Senators Packwood, Javits, and Nelson, and the House of Representatives Bill HR-11590 sponsored by Representative Steiger for the exclusion of employer educational assistance from the gross income of employees for tax purposes. Clearly, the passage of such legislation is vital to the development of effective educational programs.

CONTINUED DEVELOPMENT

There is need for more research and development in the technology used in the production of x-ray images. Greater sensitivity in sensors will help advance the potential for reducing even further the dose of x-rays associated with a computed tomographic scan. It is particularly important that the federal agencies be readily aware of their important role in the continued development of health care technologies such as that found in the computed tomographic scanner. The competition for the survival of a company in such a high technology area is intense. It is difficult for a company to recover the costs of each technological development when it is forced to continually develop its product line or lose out in the market place.

Federal assistance in the development of improvements in the computed tomographic scanners could be helpful, if not essential, particularly if it were given with adequate patent and investment protection.

In addition to the continued development of the computed tomographic scanner technology leading to realtime scans, it is important to carefully consider incentives for the continued improvement of conventional x-ray technology. The technology exists today to control x-ray techniques and x-ray emissions so that each patient receives only the minimal amount of radiation to produce the image needed for a diagnosis. Techniques exist to ensure the operation and calibration of the x-ray machine prior to the emission of energy to the patient. Quality control methods are available to maintain film processing quality and thus minimize the need for retakes due to poor development procedures. We do not advocate regulating these improvements, but rather that the reimbursement and federal aid system be tailored to provide incentives for those who choose to improve their radiological services through training, certification, good practice, and responsive equipment improvement.

I encourage the committee to urge the cognizant federal agencies to convene a study panel with broad representation, including that of engineering and the x-ray research and development community, to establish reasonable goals and objectives for the continued improvement of x-ray equipment and procedures. Such a panel should also be charged with the development of incentives to encourage the improvement in both equipment and operational procedures. The IEEE is ready to support such a study panel. An important consideration in the formulation of such a panel is the assurance of knowledgeable engineering participation.

Such incentives might take the form of preferential third party and governmental payment schedules for organizations that continue to improve their diagnostic imaging services in a manner to promote better patient care along with reductions in the exposure to radiation and the cost per procedure.

REDUCTION IN THE NUMBER OF X-RAYS ORDERED

There are various estimates of the number of x-ray images produced in excess of those required for a proper diagnosis. A recent study by the BRH (12) shows that from 5 to [illegible]0 percent of the x-rays must be retaken, largely due to technique and operator reasons. An additional unknown number of x-rays are taken to insure that every measure possible has been employed to make a thorough diagnosis in these times of increasing malpractice expense. Other x-rays are ordered to confirm a questionable diagnosis where more conservative treatment might negate the need for such x-rays.

An underlying consideration seems to be the low cost and convenience of a conventional x-ray. It is easy to see how one more x-ray requiring a few seconds of time and little materials could be considered as a high benefit payoff with only minimal cost. Such practices assume that the cost of radiation exposure is largely negligible, but until pertinent data on the risks from low levels of ionizing radiation are developed, this assumption may no longer be valid. Taking one film plate at a time, the radiation exposure could be negligible when compared with the benefits of a speedy diagnosis. However, when one considers the total aggregate expense, each additional x-ray must be closely evaluated to determine the patient benefit in comparison to the patient exposure risk.

I encourage the radiological professionals to carefully consider modifying the current procedure of automatically ordering all views in a diagnostic series when it may be feasible to make a positive diagnosis with far fewer exposures. Such a procedure would expose the patient to the minimal number of x-radiations consistent with and adequate diagnosis, rather than simply apply a uniform examination schedule for all patients. Thus, as soon as a positive diagnosis is made, the patient would no longer be subjected to additional radiation exposure. If upon examination of such a survey film, a negative diagnosis is detected, then additional views could be taken to verify the negative diagnosis or arrive at a positive conclusion.

This "trade-off" approach makes many assumptions, ranging from the existence of a positive diagnosis x-ray view to the availability of adequately trained personnel to perform the procedure. Clearly, the all views for all persons approach is simple, even though it may produce redundant and thereby potentially needless information.

A common practice in dentistry is to take a set of x-rays for all patients even if a current set is available. While such a practice is justified as ensuring a uniform quality of all x-rays, it does lead to the production of more x-ray exposure than might be required by the specific complaint. Clearly, further education of the practitioner is an important step in altering this procedure.

Mention has been made previously about the concern for the reduction of duplicate x-rays made during the transition to the computed tomographic scanner. Our members support the responsible use of x-rays for confirmation of diagnosis but appeal for a reduction in x-rays that are not absolutely required to support a diagnosis.

ALTERNATIVE TO X-RAYS

In the January 1978 issue of the IEEE Spectrum, R. Jurgen reviewed the current status of ultrasound and other non-ionizing radiation diagnostic imaging modalities and the article is reproduced in Appendix II. A description of current diagnostic ultrasound operating principles is provided in Appendix III for your information.

The production of images through the use of ultrasound energy provides a means for static and realtime visualization of internal organs. However at the present time the image quality attainable is somewhat inferior to that obtained by x-rays. Additionally, the untrasonic technique is highly dependent on the experience and capabilities of the operator for success.

Research must continue to sharpen the beam width, to better handle scattering from tissue interfaces, and to more clearly understand the changes introducing ultrasonic radiation into the tissues of the body. There is an easily developed theory that says that all external energy is detrimental to body tissues. Carried to the extreme, this theory would have us all placed in rooms where the temperature, sound level, electromagnetic environment, and even the atmospheric conditions are controlled. But more practically it seems apparent that there is a level around which our bodily systems can tolerate the introduction of certain energies without disturbing the functional equilibrium of the body tissue. The effects of ultrasonic energy are under evaluation and it appears that levels of energy normally associated with ultrasonic diagnostic equipment is below the level of the accepted tissue dosage threshold.

The attraction of thermography is that the measurement is made using inherent body energy and thus is a passive technique. Thermography has become a popular diagnostic tool for the evaluation of disorders that create surface localized hot regions. Thermography has been applied to the examination of the breast with mixed results.

Improvements in the techniques and instrumentation are essential if this procedure is to find adoption in diagnostic imaging. However, the passive thermographic technique has inherent limitations in the image resolution possible. First, the thermal energy produced by a disorder must be conducted to the surface of the skin in a manner that will facilitate identification of the disorder. Additionally, the sensitivity of the detectors must be further improved to more clearly delineate the outline of the disorder under study.

A major attraction of the thermographic techniques is their inherent suitability to programs of mass screening. With additional research and development they may reach that desired goal.

CONCLUSION

In summary the IEEE urges this committee to carefully evaluate the input of additional regulations on the development of new technology and equipment for improved health care delivery. We call for a consensus panel of engineers, scientists and medical practitioners to optimize the effectiveness of present and proposed regulations. The IEEE supports, indeed, is in a position to aid greater, in-depth training of radiology allied personnel. We believe that this approach will serve the public need more effectively in reducing needless medical x-ray exposure while containing health care costs to a reasonable level than overly restrictive and costly regulations. Federal regulatory agencies charged with the overview of ionizing radiation producing equipment should evaluate the impact that present regulations have had on the minimization of medical x-ray exposure balanced against added costs in personnel and equipment to implement these regulations. We call for the appointment of another knowledgeable panel of engineers, practitioners, and manufacturers to work with the regulatory agencies and responsible professional groups to develop methods to provide such incentives. Lastly, we strongly urge that steps be taken to keep the American public informed of the crucial developments in the science of radiology.

ACKNOWLEDGEMENTS

The author acknowledges the tremendous contribution to this statement made by several members of the Institute and in particular thankd Dr. James Hevezi, Mrs. Faye Kann, and Miss Jeanne Urlacher of the South Dakota School of Mines and Technolgy. Special thanks are given to the many associates who reviewed the drafts and their helpful suggestions are appreciated.

BIBLIOGRAPHY

(1) Report of the Secretary - 1977, Institute of Electrical and Electronics Engineers, Inc.

(2) R. K. Jurgen, IEEE Spectrum, January 1975

(3) R. K. Jurgen, IEEE Spectrum, January 1978

(4) G. N. Hounsfield, Br. J. Radiol., 46, 1016-1022, 1973

(5) S. C. Bushong, Radiologic Science for Technologists, (C.V. Mosby, St. Louis, 1975).

(6) R. E. Thomas, A Brief History of Electrical Engineering, U.S. Air Force Academy Report, (undated)

(7) N. J. Schneiders, private communication

(8) P.A. Gempel and G. H. Harris, Comparative Cost Analysis: Computed Tomography vs. Alternative Diagnostic Procedures (A.D. Little, Inc., Cambridge, Massachusetts, 1977)

(9) Hearings before the Committee on Commerce, Science, and Transportation, United States Senate, p. 263, June 1977

(10) R. K. Jurgen, IEEE Spectrum, January 1977

(11) Hearing before the Committee on Commerce, Science, and Transportation, United States Senate, p. 748 and 765, June 1977

(12) IEEE Policy and Procedures Manual, January 1978, Policy Statement 7.4-Registration of Engineers

(13) B.M. Burnett, R. J. Mazzaferro, and W.W. Church, A Study of Retakes in Radiology Departments of Two Large Hospitals, July 1975 (DHGW Publication (FDA) 76-8016)

APPENDIX I

Nowhere in the diagnostic community has innovation been so rapid as in computed tomography. The cooperation in developing safeguards in this modality by representatives of industry, university research groups, and the medical community has been astounding. The imaging method itself is an achievement in x-ray photon utilization, for the detectors utilized in CT scanning have the ability to detect every photon passing through the sensitive material, unlike film or fluoroscopic screens which allow many of the photons to proceed undetected. The CT images presented for diagnosis represent the greatest amount of information achievable at the lowest possible radiation exposure in diagnosis. Again, the balance between information content in the image and radiation exposure, represents are innovation in daignosis contributed by the technological research and development community. The contribution came directly from photographic science and technology where image information content was quantitated in terms of parameters that could easily be applied to radiologic imaging. Such parameters as resolution, sharpness, noise and speed are all parameters used in disciplines other than medicine, but their incorporation into diagnostic imaging provided a basis for the balance of image quality and radiation exposure. These parameters are directly manipulated in computed tomography. This balance implies further balance between cost of equipment and imaging apparatus, the benefit accruing to the patient in an accurate diagnosis of pathology, and the risk to both patient and radiologist through the use of x-rays to obtain the information. Balancing these three parameters is the aim of any individual or agency concerned with delivering good diagnostic health care to the individual patient.

COMPUTED TOMOGRAPHY

Perhaps the most costly piece of equipment in the diagnostic radiological profession is the CT scanner. Compared to the $100,000 one would pay for radiographic or fluoroseopic equipment, these systems represent investments of $400-700,000 per unit by x-ray departments. What makes this costly piece of equipment so invaluable to an x-ray department? Insight into the method of image production in CT scanners will shed some light on this question.

Conventional radiography consists of projecting onto a two-dimensional recording medium (usually film), three-dimensional anatomic structures. The internal structures modulate the uniform incident x-ray beam according to their thickness and radiodensity such that upon development, a grey scale image is produced which corresponds point by point to the three-dimensional body part. If bone, for example, lies within the line of sight of a soft tissue structure of interest, the soft tissue information will be lost unless a second projected image is produced oblique to the first. However, dimensional data will suffer from the same limitations as the first. In addition, the eye-brain combination of the radiologist is forced to separate often subtle densities on the final image to arrive at a three-dimensional conceptual image of the structure of interest. It is indeed a tribute to the trained radiologist that he has the ability to diagnose pathologic conditions in spite of often poor radiocontrast in the examined structure.

Conventional tomography is able to radiographically image single planes in the body by a judiciously chosen movement of the x-ray source-film screen combination during exposure. This ability is a result of film's integration over time of the radiation falling on it so that structures outside of the plane of interest (the fulchrum plane) are effectively blurred during exposure. The blurred structures, however, are still superimposed on the structures of interest reducing the ultimate contrast achievable.

Computed tomography circumvents several of these limitations and has the very real advantage of being much more sensitive to the subtle variations in body tissues that film, as a detector of radiation, cannot approach. It performs this feat, moreover, without the invasiveness of contrast media which is necessary to enhance (or at times produce) radiocontrast in many radiologic procedures. Unlike conventional tomography which images single saggital planes in the body, computed tomographic images are thin transverse planar images through the body wihtout interfering structures from other planes.

How are these transverse images constructed in computed tomography? Very simply, a source of collimated x-rays are allowed to pass through a given direction through the patient and be incident on a similarly collimated sensitive x-ray detector. The detector puts out an electrical signal which is proportional to the number of x-rays falling on it. This signal is fed to a computer which is the heart of the CT system. The thin beam of x-rays is scanned in the transverse plane and rotated until enough measurements have been taken to enable the computer to generate an image of the section examined.

To gain insight into how this is accomplished and why a computer is necessary, let's examine the x-ray beam as it passes through the patient on the way to the detector. In its traverse through the patient, the x-ray photons comprising the beam undergo all of the usual interactions with anatomic structures (scattering, absorption, etc.). This has the net effect of attenuating (reducing) the intensity of x-rays incident on the detector and the attenuating properties of the elements in the beam's path are a property of each element called the linear attenuation coefficient. In practice, the path through the patient is divided up into small elements, called pixels, with each element having its own linear attenuation coefficient. This coefficient is proportional to the radiodensity in each pixel and is the unknown quantity to be determined in CT. With many passes of the x-ray beam through the transverse plane under examination, the computer calculates the attenuation coefficients and assigns a particular value to each pixel. These values were originally called EMI numbers (after the Company that first introduced this type of imaging to radiology), but are now generically referred to as CT numbers. The numbers may be displayed on a grid corresponding to the transverse section examined. Water density is usually assigned a value of zero, with those densities less than water (air in lung, for example) being assigned negative numbers, and those with higher densities (bone) positive CT numbers. Each value is assigned an adjustable shade of grey and displayed on an oscilloscope or TV monitor. It is this image that is adjusted for diagnostic clarity. Hard copies of the displayed image may be made with available camera systems for archival storage or used in discussing a patient study. The computer in arriving at these values often performs over 100,000 separate calculations, a job it does easily.

The power of computed tomography is its ability to separate less than 1-2% differences between pixels. Over the five year period between the introduction of computed tomography and the present time, the equipment has become more reliable and the time for single scans has been reduced from over

4 minutes to just under 5 seconds. This scan time reduction has been made possible through the introduction of miltidetector systems, and fan beam geometry. Thus, instead of a single pencil-thin beam of x-rays, the present generation of scanners utilize a circular array of detectors closely spaced such that over 300 simultaneous measurements may be made. Scan times may be reduced only so far in present technology, however, since the accuracy in the determination of the CT numbers is a function of the number of x-rays transmitted in each scan line and detected. Both the number of elementary cubicles that one choses to divide the transverse section and the scan time have a profound effect on image quality.

There are basically three parameters that affect image quality in computed tomography. They are image element size (resolution), scan time, and number of x-rays detected per scan line (accuracy). To complicate conditions further, varying any one of these affects the others.

Resolution is specified when one chooses the collimating aperture size on the detector, not the source. For an image element size in a transverse slice of 1 x 1 millimeter in the patient, the collimating aperture on the detector varies from 1 x 8mm to 1 x 17mm on most commercial equipment. The latter dimension determines the transverse slice thickness and is adjusted to allow more x-rays into the detector for greater accuracy. Hence, the pixels actually represent the average attenuation coefficient in a volume 1 x 1 x 10mm (if the slice thickness is 10mm). For example, if a 0.1mm diameter calcific deposit were to occur somewhere in one of these boxes, its attenuation value would be averaged with the rest of the soft tissue values in the box and the displayed image element would appear as soft tissue. This is the reason that CT applied to high resolution exams like mammography do not work well at present.

Scan times on commercial CT equipment have been consistently lowered over the years from 4 minutes or more per scan to just under 5 seconds. This great reduction in scan time, which removes motion artifacts from the images, has been accomplished by two major innovations. First, the number of detectors has been increased from one or two to more than three hundred. This means that for a given position of the x-ray source, over three hundred simultaneous measurements may be made. However, with the "multidetector" systems, the scan lines are not parallel to one another but diverge from the source to the detector in a fan-like array. The source and detectors rotate around the transverse section of the patient under examination and produce an image in a fraction of the time necessary for the outmoded single detector sytems. The problem of more rays incident on the pixels with sections closest to the source is solved in the computer algorithm. Although the next breakthrough in scan time appears to be a real time system, the requirement that a minimum amount of time be spent at each source position in order to collect enough x-rays for accurate determination of the CT numbers, makes this system unfeasible at the present time. However, it points to the next indicator of CT image quality, namely accuracy. The accuracy with which the CT numbers are determined depends directly on the number of x-rays detected at each position. The higher the accuracy, the greater the number of x-rays that must be detected. It is easy to see the interdependency of these image quality parameters in this light. To collect more x-rays in the detectors for greater accuracy, the scan time must increase. If greater resolution is desired, the pixel size may be halved but with the same scan time the accuracy in each pixel will be less. An do on for other changes in the parameters.

One of the byproducts of CT imagery that has plagued conventional radiography over the years is the elimination of scattered radiation -- automatically by the method of production. In the fast scan fan beam systems, some scattered radiation may reach the detectors but its effect is much less than on other radiologic images.

In summary, computerized tomography offers a means of imaging anatomic structures in a most highly efficient manner. Its introduction in the radiologic armamentarium will have a similar impact in the medical community as the discovery of the x-ray by Roentgen before the turn of the century.

APPENDIX II

Electronics in medicine

Diagnostic imaging advances; microprocessors aid laser systems, prostheses

Ronald K. Jurgon Editorial Director

Diagnostic imaging

Amid universal concern over ever-increasing health-care costs and growing concern over technology's effect on those costs, biomedical engineering continues to make significant progress. Techniques for various diagnostic imaging modalities are still in the limelight. Transmission computer tomographic (CT) scanners with faster scans and variations of scanning schemes have been introduced. Making their commercial debut last year were emission CT scanners that use positron-emitting radionuclides or radiopharmaceuticals injected into, or swallowed by, a patient to permit tracing of metabolic processes. And ultrasonic imaging was further refined with improved detectors and scanning techniques. As imaging techniques become more sophisticated, they push the state of the art in computers, array processors, detectors, and data storage.

CCDs

Lasers

Recently developed solid-state devices, such as charge-coupled devices (CCDs), are being used—at least experimentally—in medical instrumentation. And important gains have been made in applying microprocessors to medical instruments, in laser applications in medicine, and in devices for the handicapped.

Device regulation

Wary medical-device manufacturers are following with intense interest the actions of the Bureau of Medical Devices of the U.S. Food and Drug Administration (FDA) as it comes to grips with its mandated role in regulating medical devices under the Medical Device Amendments of 1976. By the end of 1977, medical-device manufacturers had registered as such with the FDA and were completing listings of the devices they manufactured. During the year, the FDA issued final regulations on hearing aids, intrauterine devices, intraocular lenses and establishment of registration and premarket notification. Fears on the part of manufacturers were being allayed, or confirmed, as the regulatory process evolved. But questions were being answered, forms of compliance were taking shape, and the job was being done.

CT scans: how fast is fast enough?

CT scanners

Therapy planning

Since the first CT scanner was installed in a London hospital in 1971, technological progress in these scanners has been rapid and dramatic. Perhaps most significant is the reduction in scanning time. The first-generation scanners took more than 4 minutes to complete a scan of the human head. When scanning times dropped to 20 seconds or less, body scans became possible because patients were able to hold their breaths during the examination. Newer scanners now operate with scan times as low as 2-3 seconds and, in the laboratories, 100-millisecond scanners are under development.

The significance of extremely low scan times is that they make dynamic CT scanning possible. When scanners become available with 50–100-millisecond scan times, it will be possible to study blood flow and to "freeze" the heart. Some researchers feel that the ultimate use of CT scanners may be in cardiology where, for example, heart-disease-prone patients might be mass screened to diagnose early indications of heart problems. At present, a heart attack is often the first symptom.

Scan times have been reduced, in most cases, by changes in the mechanical features of CT scanners. For example, the first CT scanner used a highly collimated X-ray beam moved laterally across the patient's head. The X-ray tube and single detector were moved in increments of one degree through a total of 180 degrees. Total scanning time was more than 4 minutes. Two detectors used side by side in the same basic setup reduced examination time by making it possible to study two adjacent axial slices simultaneously. Yet another improvement was to use a broader X-ray beam and multiple detectors. With 30 detectors exposed to a 10-degree beam, for example, only 18 rotations in 10-degree increments were necessary. This technique cut scan times to about 20 seconds. By using a wide fan that covers the entire cross section of the body, it is possible to eliminate the transverse motion and scan by pure rotation of the X-ray source and detector array through an angle of 220–360 degrees. Scan times as short as 3 seconds have been achieved in this manner.

The new EMI Medical Inc. 7000 general diagnostic CT scanner attains 3-second scanning speeds by employing approximately 1100 solid-state detectors in a ring close to the patient's body. As a fan-beam X-ray source rotates outside the sensors, the near side of the sensor ring edges away (nutates) from the path of the photon beam. The beam fans only on those detectors that are beyond the patient's body.

Less dramatic, but equally as important as reductions in scan times, are other improvements in CT scanners. As experience is gained in using the scanners, improved techniques are evolving for data processing. One of several techniques already on the market is Technicare Corporation's Ohio-Nuclear Division's radiation-therapy planning system called Deltaplan. It consists of a computer that is fed images directly from the floppy disk of a CT scanner, as indicated in Fig. 1. The Deltaplan computer analyzes the images and produces programs that allow the radiation-therapy physician to develop extremely accurate treatment plans focusing on diseased tissue and minimizing irradiation of healthy tissue. The system was developed jointly by Ohio-Nuclear and Memorial Sloan-Kettering Cancer Center in New York City.

CT scanners, rightly or wrongly, have become the favorite target of those who feel that technology is a major contributing factor to rising health-care costs. They have achieved this dubious distinction because most of them are expensive initially ($375 000 to $700 000), expensive to operate ($200 000 to $375 000 per year), and expensive for patients ($150 to $250 per CT scan). To add fuel to the cause of the anti-CTers, the scanners are extremely popular and manufacturers are hard pressed to keep up with orders from hospitals, clinics, and physicians. So questions have been, and continue to be, raised about their efficacy—even about the definition of the efficacy in the CT context—and whether that efficacy, or lack of it, is worth the added health-care cost.

There is some indication, however, that prices may come down. For example, Ohio-Nuclear has a CT scanner that sells for $95 000, Omnimedical has one for $119 000, and EMI has one for $129 000.

Recovering costs

Ironically, despite the high prices of CT scanners, manufacturers are finding it difficult to recover developmental costs. The technology is so fast moving that, to remain competitive, a manufacturer has to bring out a new model before developmental costs of previous models are recovered fully. And, with only a handful of CT scanner manufacturers left who can cope with the peculiarities of the market, a shake-out may be in the offing.

Scanning in a van

Often suggested as a means for minimizing the burden imposed on health-care costs by the proliferation of CT scanners is the restriction on the number of scanners in any particular geographic area. However, this approach can lead to problems. One is the need to transport a patient by ambulance from a hospital that has no CT scanning facility at a cost to the patient that can often exceed the cost of the CT scan. EMI Medical Inc. of Northbrook, Ill., has another answer: a compact hospital scanning system on wheels that makes it possible for several hospitals to share a CT scanner. A van is equipped with an EMI CT1010 head scanner and a separate control room for the operator. While the van is at a hospital, a radiologist, using equipment on the vehicle, views each patient's scans, interprets the results, and communicates them to the attending physicians. The system is already serving three hospitals in the Los Angeles area and a unit has been delivered to American Medical International, Inc., a health-care-services company that operates more than 50 hospitals in the United States, Europe, and South America.

Enter the emission CT scanner

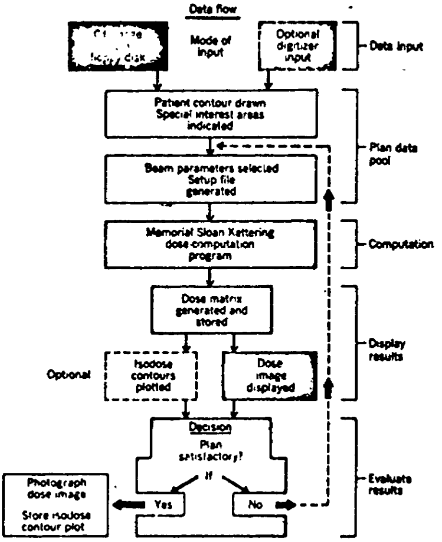
Newest entrant in the CT scanning field is the emission CT scanner. Instead of X rays, it uses radionuclides or radiopharmaceuticals. Unlike the X-ray transmission CT scanner, which measures attenuation of the X-ray beam by body structures, the emission CT scanner traces the biochemistry of the body in picture form and has been used to assess metabolism and blood flow in the brain and heart, among other applications. One possible disadvantage of the emission CT scanner's use of positron-emitting radioisotopes is the need for an on-site cyclotron. Announcements of emission CT scanner developments in 1977 came from, among others, Oak Ridge Associated Universities and EG&G, Inc.; G. D. Searle & Co., and the Union Carbide Corporation.

The EG&G Ortec emission CT scanner (Fig. 2) measures and locates the concentration of a positron-emitting radiopharmaceutical that is administered to the patient and is distributed through the body according to known physiological phenomena. When a positron annihilates, two gamma rays are emitted in opposite directions. Opposing detector banks detect the coincident gamma rays and provide a sensitivity to the direction from which they were radiated. The emission CT scanner compiles and sorts these data in its computer and generates a tomographic image representing the metabolic activity occurring within a "slice" through the patient.

The basic emission CT scanner shown in Fig. 2 includes the scanning unit; a data-acquisition system; and the associated computer, displays, and data-storage system. The scanning frame contains 66 NaI(Tl) detectors, 11 on each side of a hexagonal array. Computer-controlled stepping motors scan the detectors along the sides of the hexagon. The entire array is rotated through 60 degrees during the course of a normal scan. Signals from each of the 66 detectors are amplified and processed to detect coincident pulses between detectors on opposite sides of the hexagon. These coincident events are counted, with a separate counting channel for each detector pair. The data are transferred to the computer at the end of each counting interval.

The first EG&G emission CT scanner is in operation at U.C.L.A.'s School of Medicine, where it is used predominantly for patient diagnosis, for study of the human brain and heart. A second EG&G emission CT scanner is slated for the Oak Ridge Associated Universities, where it will be employed in research programs being conducted to evaluate radioisotopes developed as basic tools for

[1] Radiation-therapy planning for cancer treatment can be performed directly on high-resolution CT scanner images through use of the Deltaplan system. Beam orientation is accomplished interactively on a video screen to permit maximum placement accuracy and optimum dose distribution.



BEST COPY AVAILABLE

cancer diagnosis.

G. D. Searle's emission CT scanner uses standard radiopharmaceuticals instead of positrons. It is under clinical trials at St. Luke's Episcopal Hospital in association with Baylor University College of Medicine.

Ultrasonic diagnosis

Ultrasonic diagnosis forges ahead

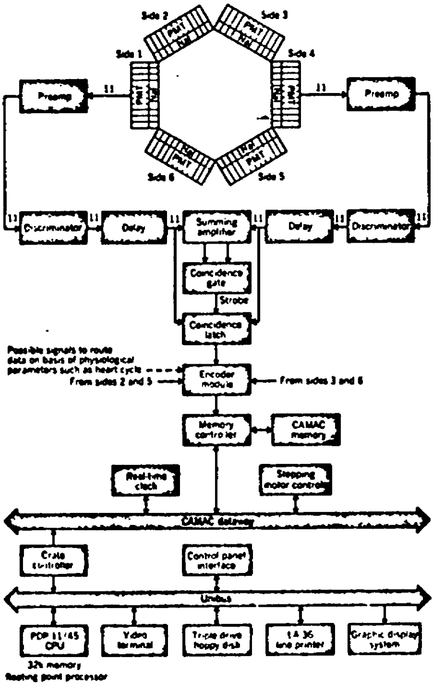
ULISYS

Ultrasonic diagnostic techniques continue to expand their horizons and to become more and more sophisticated in device design, with switched linear arrays, mechanical sector scanning, phased-array scanning, and incorporation of state-of-the-art solid-state developments.

A-, B-, and C-scans

One interesting new development is Searle Ultrasound's Digi/Sonic digital scan converter, a device for transforming ultrasonic echoes into visual images of soft tissue. The converter is a solid-state digital-image memory that is said to allow improved image processing—including high resolution, more rapid electronic writing speed, and added image stability compared with analog scan converters commonly used. The digital scan converter is also said to open the way for real-time computerized image processing. The new converter translates ultrasonic echoes into numerical intensity values ranging from 0 to 30 at each of more than 260 000 points on an electronic matrix. This numerical value accurately establishes a brightness level for each point when the scan information is transferred to the screen.

[2] EG&G's emission CT scanner consists of the components shown. The scanner generates a tomographic image representing the metabolic activity occurring within a slice through the patient. Such images aid the physician in the diagnosis and treatment of malignancies, heart attacks, strokes, and other body ailments.



At Stanford Electronics Laboratories' Integrated Circuits Laboratory, LSI techniques are being applied to the development of an ultrasonic imaging system called ULISYS, for use in medical diagnosis. It involves powerful ultrasonic probe assemblies, including a 16×16-element piezoelectric transducer array, a new multiplexer matrix, and corresponding signal processors and controllers. The ultrasonic system has the capability of producing amplitude-vs.-time (A-scan) and intensity-vs.-time (B-scan) displays for any row or column of transducer elements and intensity-vs.-position (C-scan) displays for the entire array. The system is being evaluated clinically by the Department of Cardiology at the Stanford University Hospital.

CCD electronic lens

Also at the Integrated Circuits Laboratory, work is underway on a second generation of specialized ultrasonic imaging systems that includes an electronically focused and beam-steered, deep-body imaging system and an electronically scanned near-field, superficial-organ imaging system. The deep-body system uses a Stanford-invented C3D charge-coupled-device electronic lens (Fig. 3) and the theta transducer array to realize high resolution in all three spacial dimensions. The system is designed for cardiac and abdominal imaging.

Imaging by nuclear magnetic resonance

Yet another noninvasive imaging technique that holds promise for clinical use with humans is imaging by nuclear magnetic resonance (NMR). In NMR, the resonance frequency is directly proportional to the magnetic field in which the nuclei are immersed. Another characteristic is that the signal is extremely sharp. These properties enable NMR to be used to determine the interior distribution of protons or other nuclei in objects. One-dimensional profiles of nuclear density can give information about the internal structure of a three-dimensional object, such as the human body. The technique is capable of responding well to fluid and soft tissues and it can discriminate between tissues of similar atomic density through their differing relaxation times. It can also measure diffusion and fluid flow.

Some researchers are hopeful that, in the next year or two, useful images of interiors of the human body will be produced by NMR imaging techniques. If so, X rays, ultrasound, and radioisotopes may have another rival, or perhaps more accurately, another complementary tool.

Raymond Damadian of Brooklyn's Downstate Medical Center hopes to prove that NMR techniques can be used to detect and perhaps treat human cancer. So far, he's been able to show that NMR can detect differences between healthy tissues and some kinds of cancerous tissues and can detect a tumor in a living animal. The hoped for breakthrough will be in applying the technique to humans.

Imaging techniques: allies not enemies

The various imaging modalities in clinical use, to the unitiated, present what seems to be a competing arena of technological advances. In reality, however, the techniques are more complementary than competitive. In a recent article in *Radiology* (Aug. 1977, p. 387), P. J. Bryan *et al.* compare CT scanning, ultrasonic diagnosis, and nuclear imaging for application in detecting space-occupying processes in the liver. The article summarizes experience with 80 patients, of whom 29 lacked unequivocal evidence of the nature of the abnormality. Of the 51 remaining patients, ten were considered to have normal livers with defects of extrinsic origin, 36 had solid hepatic tumors, and four had simple cysts. There was one amebic abscess.

The three imaging techniques were assessed and rated on a scale of 0 to 5 according to the clarity with which the intrahepatic lesion was delineated. Ultrasonography scored the highest, with a mean of 3.5. CT scanning rated second with 3.15. Nuclear imaging (scintiscanning) scored 2.9.

Although the authors do not say so specifically, the article may imply that there is value in combining several modalities in one instrument with multisensors. Such an instrument would give a physician more information than any one of three separate displays and would represent lower capital and operating costs for a hospital as compared with three separate facilities.

What about microprocessors?

Microprocessors in medical instruments did not receive as much overt attention in 1977 as in the last several years, but that lack of attention was not representative of industry activity. If they were not as newsworthy as they had been, it may only be indicative of the fact that such microprocessor applications were becoming commonplace. In addition to making possible portable devices such as automatic blood-pressure cuff monitors and ambulatory ECG (Holter) monitors, microprocessors are enabling the development of sophisticated devices for use in clinical applications.

One such application reported last year, by P. G. Katma *et al.* in the *IEEE Transactions on Biomedical Engineering* (Nov. 1977, p. 536), is a microprocessor-controlled memory for cardiopulmonary monitoring of high-risk infants. It is used for delaying waveforms, operated in conjunction with commercially available vital-signs monitors and recorders, and was developed to generate a concise record of apneic and bradycardic episodes during long-term monitoring of premature infants and infants who have been hospitalized during the first few months of their lives because they had stopped breathing and/or turned blue at home. The system provides a visual recording of only the potentially life-threatening episodes in continuously monitored infants.

By using a large semiconductor memory, the device allows the recording of physiological waveforms prior to the occurrence of alarm conditions. The semiconductor memory system, shown in Fig. 4, uses an Intel 8080 microprocessor controlling a 32k, 8-bit Monolithic Systems Monostore VII Planar random-access memory. The microprocessor sequentially samples four input channels through a multiplexed A/D converter and stores the samples in the RAM.

Lasers in medicine

Surgical instruments and human-eye tests are common applications for lasers in medicine. Carbon dioxide lasers are being used for surgery in confined spaces, such as in surgery of the larynx or of precancerous conditions of the vagina, and in the removal of rectal polyps. And plastic surgeons at Beth Israel Hospital in Boston are using a laser to treat a type of birthmark called a hemangioma.

A new instrument called a retinal visual acuity tester utilizes a laser to permit the instrument operator to evaluate quickly and easily the functioning of a patient's retina-to-brain visual communications link. Manufactured by Acuity Systems Inc of Reston, Va., the instrument's laser disregards all refractive error in the eye and reads through any damaged or opaque media. The instrument determines what the eye is capable of seeing, based on an evaluation of the primary vision mechanisms. This information is a valuable aid to a physician with a patient who is a poor responder or who has problem refractions. For surgeons, the instrument is useful in evaluating a patient's likely visual acuity after such operations as cataract extraction, corneal transplant, or vitreous surgery.

More aids for the handicapped

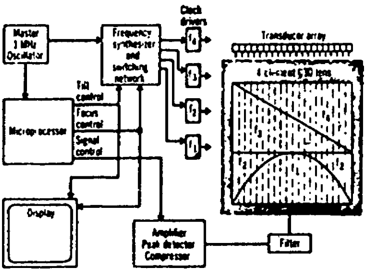
The wonders of technology in developing aids for the handicapped do not always result in those devices reaching the handicapped. Fortunately, one major effort in this direction took place in 1977, when the Telephone Pioneers of America demonstrated more than 20 communication, teaching, and recreational aids for handicapped children and adults. The devices are available nationwide in the U.S.; inquirers should contact the

Lasers

Super diagnoser

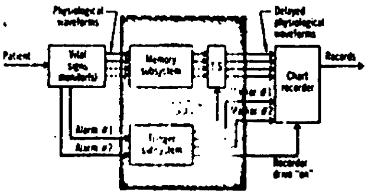
Aiding the handicapped

Microprocessors



[3] System incorporating a CCD lens takes measurements in ultrasonic tests and provides real-time delay-line-focus and beam-steer electronics in a single IC package.

[4] Memory device (within dashed rules) is interconnected with commercially available system components in a microprocessor-controlled memory for cardiopulmonary monitoring of high-risk infants.



BEST COPY AVAILABLE

For further reading

An insight into transmission CT scanners, both technically and from the viewpoint of the overall health-care system, can be obtained from the following publications

An excellent summary of the progress in CT scanners is reported by Bryan R. Westerman of EMI Medical Inc. in his paper, "Principles and developments in transmission C.T.," presented at MIDCON '77. The paper is available in Session Reprint 10, "Methods of Diagnostic Imaging in Medicine."

Aneurysm detector

CT scanners and the health-care system are treated in three interesting reports. A policy statement, "Computed tomographic scanning," April 1977, issued by the National Academy of Sciences, Washington, D.C.; "CT in perspective: diagnostic efficacy and health care implementation," August 1977, EMI Medical Inc.; and an article in the July 28, 1977, issue of *The New England Journal of Medicine*, pp. 216–218, by J. E. Fielding and P. X. Russo, entitled, "CT scanners: distribution and planning status in the United States."

Valuable advice on medical-device regulations is available in a newly published booklet, "Everything you always wanted to know about the medical device amendments . . . and weren't afraid to ask." It may be obtained from the Bureau of Medical Devices (HFX-132), U.S. Food and Drug Administration, 8757 Georgia Avenue, Silver Spring, Md. 20910.

Prosthetics

Telephone Pioneers of America, in care of the local telephone company. All of the devices are developed and manufactured by Pioneer volunteers on their own time, and are donated or provided at cost to schools, hospitals, and clinics, and to handicapped individuals who need them.

Among newly introduced aids are: a modified transistor radio that amplifies television programs for the deaf, a "talking animal" that encourages responses from autistic children; a light probe that enables a blind person to "hear" light; a voice-activated telephone for the severely motion-impaired; a money-saving telephone and data-terminal hookup that allows homebound stroke patients to receive therapy from a hospital pathologist miles away; a "climbing squirrel" that encourages speech in profundly deaf children; and a device that enables speech-impaired students to communicate with teachers by activating flashing lights on a wooden board.

Spoken-word devices

Also last year, HC Electronics, Inc., a subsidiary of the American Hospital Supply Corporation, introduced a hand-held, battery-operated electronic voice system for nonverbal/nonvocal children and adults. Developed by Votrax, the Phonic Mirror HandiVoice simulates the human voice, produces complete sentences, and reproduces virtually every word in the English language. Its unlimited vocabulary is attributable to its use of 45 phonemes, or basic sound elements, rather than words. Two versions of the device will be available for delivery in April. The HC 120 features a numeric keyboard and liquid crystal display, similar to a pocket calculator, with vocabulary selections made via three-digit numeric codes. It is designed primarily for those individuals with lower motor skills and higher cognitive skills. The HC 110 features a touch sensitive display board with 128 stations which can be represented as words, pictures, or symbols. It is designed primarily for those individuals with lower cognitive skills and higher motor skills. For those with some reading skills, words can be printed on the display board. For others, pictures or symbols can be used.

Still in the laboratories are other voice-output devices for the handicapped. For example, Telesensory Systems Inc. is working on a spoken-word output version of its Optacon reading device for the blind. And Smith-Kettlewell is researching a spoken-word device for reading data from a TV monitor display.

And other developments in brief

- The University of Cincinnati Medical Center has developed a stethoscope-computer system that can detect sounds that warn of the presence of a cerebral aneurysm. It is based on the fact that an aneurysm's vibration produces a musical tone.
- A U.C.L.A. engineering professor has developed a new type of hearing unit for people whose deafness to high-frequency sounds cannot be remedied by conventional hearing aids. It makes use of frequency-compression techniques.
- Beckman Instruments, Inc., has developed a new laboratory instrument that uses an advanced light-scatter measurement technique to detect protein abnormalities indicative of diseases ranging from bone cancer to emphysema.
- Systemteknik AB of Sweden has available commercially a myoelectrically controlled hand for two- to five-year-old children. The miniaturized prosthetic hand, which provides opening and closing of the fingers, works on the same principles as adult-size versions that have been available for several years. The new hand will enable children with congenital below-elbow deformations to benefit from "adult" technology.
- A research group working at Children's Hospital Medical Center in Boston and Liberty Mutual Research Center in Hopkinton, Mass., has developed an electrode unit capable of detecting voluntarily elicited motor signals for prolonged periods of time. The electrode unit is designed to be implanted around severed peripheral nerves, to detect the neuroelectric signal on the surface of the nerve, and to convey the signal outside the body. Thus far the electrode has been implanted in animals with successful results and, in its present form, may prove suitable for implantation in humans. Additional tests are required to better understand the physiological effects of the electrode on the enclosed portion of the peripheral nerve. The main purpose for developing the electrode has been to obtain neuroelectric signals that can be used to control an upper-limb prosthesis. The motion of a prothesis activated in this manner would be "volitional" and "natural." The individual would merely desire a particular sequence of movements in order to initiate a chain of events beginning in the brain and ending with appropriate movement of the prothesis. ◆

Information for this article came from many sources. Major contributors were E. Alpert, J. Cooper, and R. S. Newbower, Massachusetts General Hospital; J. C. Bliss, Telesensory Systems, Inc.; D. Boyd and P. Callen, Moffitt Hospital, University of California; J. Brady and W. White, G. D. Searle & Co.; C. De Luca, Childrens Hospital Medical Center (Boston); M. Eden and W. Frieuf, National Institutes of Health; T. Estrin, University of California; J. Knuth and R. Melen, Stanford Electronics Laboratory; J. Moore, EMI Medical Inc.; L. Pilot, U.S. Food and Drug Administration; L. A. Scadden, Smith-Kettlewell Institute of Visual Sciences; H. Sherman, The Harvard School of Public Health.

APPENDIX III

Since diagnostic ultrasound seems at the present time to offer the most lucrative potential for replacing many diagnostic procedures presently using ionizing radiation to produce an image, this appendix will deal with its characteristics.

DIAGNOSTIC ULTRASOUND

This modality was introduced into diagnotic medicine in the late 1940's but was relegated to a research tool until the late 1960's when a resurgence in its use in clinical diagnostic medicine was made possible by the invention of the image storage tube. To become familiar with this imaging modality, a brief discussion of its use in diagnostic radiology follows.

Ultrasound is acoustic energy propagated in the form of longitudinal waves. Unlike electromagnetic waves which are transverse in nature and can travel in a vacuum, acoustic waves require matter for propagation and may be viewed as alternating compression and rarefaction of the propagating medium in the direction of the ultrasonic beam. Acoustic frequencies utilized in medical diagnosis have been limited to the range from 1-15MHz, values far above the audible range. These waves travel through matter with a velocity characteristic of the medium; the average value for tissue is 1540 meters per second. Hence, the acoustic wavelength in tissue is limited to the range from 1.5-0.1mm. These values correspond to the theoretical limit of resolution in acoustic imaging. Proportionately better resolution is achieved by using higher frequencies, but the depth of penetration of the beam decreases as the frequency is increased and a compromise between resolution and depth of visualization must be accepted.

Pulse-echo ultrasound is the most common modality employed in diagnosis. As its name implies a short burst of acoustic energy at a fixed frequency is emitted from an acoustic transducer into the structure to be examined. The same transducer is used as a receiver to "listen" to the return echoes from structures within the body. These echoes occur at tissue interfaces within the body and are displayed as voltage pulses on an oscilloscope. Since the arrival time of an echo to the transducer in contact with the surface is proportional to the depth of the interface beneath the surface, the correct spatial relationship of echo producing interfaces will be preserved on the display. This method of presentation is the so called "A-mode" for Amplitude modulation, a term adopted from radar terminology. The echo amplitudes increase with the promixity of the echo producing interfaces to the transducer and the disparity of tissue density on either side of the interface. In pulse-echo work, the amplitude of the return echo is greatest when the interface is perpendicular to the direction of travel of the ultrasonic beam. Indeed, if the angle that the tissue interface makes with the direction of the beam is too great, no echo will be recorded for that interface.

As alluded to above, echoes will be returned to the transducer if there is a disparity of tissue characteristics on either side of the interface. These characteristics are the acoustic impedance values for tissues on either side of the interface. The acoustic impedance is the produce of the density and the velocity of sound in the medium. In particular, the air-muscle boundary reflects most of the incident acoustic energy leaving little transmitted energy for echo producing information beyond this interface. Hence, air filled body cavities present difficult structures to study ultrasonically.

In order to produce two dimensional images of structures, some electronic manipulation of the A-mode presentation is necessary. This begins with displaying the echoes as bright dots in a line (corresponding to the acoustic beam direction) on the display. The brightness of the dots are proportional to the amplitude of the return echoes, and the display forms the so-called B-mode (Brightness-modulation) presentation. B-mode is not used alone in ultrasonic imaging but the particular manipulation of the echo produced dots determines the type of scan.

In the M-mode (Motion-mode) presentation, the bright dots are swept across the display face such that moving echoes trace a curved path during the sweep. The display may be "frozen" on a storage oscilloscope and photographed for interpretive analysis. The chief application of M-mode operation is in cardiac studies where valve and other cardiac motions may be displayed and analyzed for departures from normalacy. The diagnosis of pericardial effusion is generally made at many institutions using M-mode.

With the advent of good commercial scanning equipment, compound B-mode scans are destined to be the most frequently utilized ultrasound examination because they produce a direct two-dimensional map of interfaces in the body which may be correlated with normal cross sectional anatomy. This scanning technique also begins with the basic B-mode presentation or a line of bright dots on the display corresponding to echo producing interfaces encountered within the body by the ultrasonic beam. In this method of imaging, however, the location (position and angle) of the acoustic transducer is electronically computed and displayed on the oscilloscope along with the B-mode presentation. As the transducer is moved across the body, a new set of B-mode dots will be displayed on the oscilloscope in a different position. In this way a two-dimensional map of acoustic interfaces in the body may be built up by constantly changing the position and angle of the transducer. In order that information be preserved at previous transducer positions, the image is displayed on a storage oscilloscope and subsequently photographed for permanent recording. Some coupling medium between the transducer face and patients' skin is necessary for good transmission and reception of the ultra-beam. Indeed, without this coupling medium, the first interface encountered by the ultrasound beam is the air-skin interface which returns most of the ultrasonic energy back to the transducer. Coupling gel or common mineral oil are good coupling media applied directly to the skin.

B-mode scans are commonly made by moving the transducer in contact with the surface of the body along transverse or saggital planes. By obtaining scans at 1-2 cm intervals in these planes, three-dimensional information may be extracted. In contact scanning, one has freedom in positioning the transducer such that the maximum number of interfaces are intercepted in a perpendicular direction to the beam. Non-contact scans are less common but have the advantage that the scanned object is held rigidly throughout the scan improving reproducibility and accuracy. Water is used as a coupling medium in non-contact scans and the motion of the transducer may either be of linear, sector (sweeping the transducer through a given angle) or a combination of these motions.

One of the disadvantages of compound B-mode scanning is the bi-modal presentation of the echoes. That is, independent of echo strength returning to the transducer (receiver), either the echo is displayed as a dot of constant brightness (at its appropriate position in the image) or it is not displayed at all. This method of display does not allow subtle gradations in tissue consistency to be imaged. Some flexibility is achieved in adjusting parameters such as amplifier gain to allow more or fewer echoes to be displayed. But the bi-modal presentation is a consequence of the storage oscilloscope method of display. Obviously, more information is transferred to the diagnostician if strong echoes are displayed brighter than weaker echoes with a range of brightness extending from the strongest to the weakest echoes present. On film, the echo complexes will be displayed as varying shades of grey.

One method that foreran present grey scale ultrasound consisted in the elimination of the storage oscilloscope and the substitution of a "real time" oscilloscope coupled to a camera with a long (on the order of seconds) shutter open time. The "real time" oscilloscope displayed varying brightness B-mode dots but could not store these for any convenient length of time. This was immaterial since the shutter of the camera was opened at the beginning of the scan and the film itself became the storage medium. Hence, a timed exposure during the length of the scan was produced preserving a number of shades of grey in the image. Some gradations in density are presented by this technique--much more than could be obtained with the storage oscilloscope method of display. However, several disadvantages of this technique existed and it did not come into general use. It was not until the introduction of the storage tube or scan rate converter to the field of ultrasonic imaging that this tool of the diagnostician found its present position.

Virtually all of the grey scale ultrasonic images are presently producing through the use of a unique electronic device called the scan rate converter or image storage tube. This device preserves the brightness of the B-mode echoes and displays them in good fidelity on a conventional television monitor which may be photographed for permanent recording. The image is built up (write mode) on the storage element of the scan rate converter tube as the scan proceeds. Position and angle information are simultaneously input to the horizontal and to the vertical deflection plates on the tube. When completed, the latent image exists on this sensitive element in the form of elementary electronic charges. The image may be non-destructively extracted (read mode) and input to a television monitor. This image is reproduced on the monitor screen at thirty frames per second. Hence the name scan rate converter. In present generation units, the image may be displayed as it is being built up on the storage tube allowing maximum flexibility in operator control. Contrast and latitude across the image may be varied with controls on the scan rate converteer and TV monitor. In practice, these controls are set at a specific level and contrast and echoes and through use of the TGC (Time-Gain Compensation) control. This latter control simply removes the effect of strong return echoes near the transducer and weaker echoes at large distances from the transducer. In principle, one would like to produce strong echoes at interfaces with widely differing acoustic impedances on either side, and not simply from the fact that the echo was produced near the transducer face. The TGC control enables one to amplify those echoes occurring at greater distances from the transducer proportionately. In doing so, the echo strengths, manifested as shades of grey on the final film recording, are more representative of the tissue composition in the body.

In summary, some of the methods of extracting and presenting ultrasonic information from the body have been presented. This fertile field has progressed to the point that pulse-echo ultrasound systems are in routine use in major institutions both as an adjunct to other diagnostic modalities and, frequently, as the sole method of extracting useful information. As the technology of such systems becomes more refined and our knowledge of the interaction of acoustic energy with matter increases, the future holds great promise for this diagnostic modality.

The cost of diagnostic ultrasound equipment is low compared to other radiology equipment. However its use is limited to only a few anatomical structures amenable to ultrasound diagnosis and cannot, therefore, be viewed as a modality of general utility. In addition, radiologists and radiologic technologists are only recently being trained in the use of this equipment which requires considerable skill both on production and interpretation aspects of the images. Its methodology, however, does offer a distinct advantage over ionizing radiation image production methods since the data concerning biological damage due to ultrasonic energy indicates no measurable effects at diagnostic irradiation levels (less than 10 milliwatts per square centimeter).

There are other methods of utilizing acoustic energy to produce diagnostic images but these are presently in the research stage with little clinical efficacy demonstrated at present. These are modifications of pulse-echo techniques and the use of acoustic holography to obtain diagnostic images. One method has potential for producing viable results that could have significant clinical impact if initial results are indicators. It essentially uses the image reconstruction method of computed tomography but replaces the x-ray tube with an ultrasound transmitter and the radiation detectors with acoustic receivers. Clinical research programs utilizing this approach are presently in progress at various sites across the U.S. and two in particular at the Mayo Clinic in Rochester, Minnesota, and the University of Colorado Medical Center in Denver, Colorado, have exhibited encouraging results.

Mr. ROGERS. Thank you very much, Doctor, we appreciate your testimony.

Dr. Carter.

Mr. CARTER. Thank you, Mr. Chairman.

What incentives exist in the marketplace to develop improved safety features for new X-ray machines?

Dr. GOWEN. At the present time, sir, the incentives in the marketplace as they presently exist are minimal. We propose that action be taken to develop incentives in the marketplace. Part of the incentives we suggest is for using the third-party payers.

Mr. CARTER. Could you clarify what you mean by that?

Dr. GOWEN. We are suggesting there is a need to bring incentives into the system. That there should be a way that if one uses efficacious, safe practice, that one receives a return for that. There should be an incentive in the system for it. At the present we recognize there is no incentive in the system that at least from our perspective we consider to be effective.

Mr. CARTER. What features of equipment development involve the stiffest competition? The speed of X-ray equipment or timing features?

Dr. GOWEN. You are speaking in terms of specific equipment development?

Mr. CARTER. Yes.

Dr. GOWEN. Sir, I guess I would like to say to you that I am not representing the manufacturers group. I feel that I am more in a position to discuss science and technology. Within our groups we have talked about developments. Our members speak not as corporates of the IEEE, nor do not speak to us as manufacturing groups, but as individual engineers and scientists.

Dealing with our members, their major concern is that we not waste time or money on essentially needless whistles and bells. In our statement we mention such things that have been very effective, for instance, as a result of the 1974 regulations, equipment for limiting and getting proper beam widths, covering the image receptor have been, very useful. However, some of the problems with collimation have not been useful, not near as effective, and very costly.

Mr. CARTER. Thank you very kindly.

Mr. ROGERS. How difficult is it to include in equipment so-called fail-safe devices, assuring that badly maladjusted equipment would not be used?

Dr. GOWEN. With today's technology, sir, that is rather easy to do.

Mr. ROGERS. Not too expensive?

Dr. GOWEN. And not too expensive.

Mr. ROGERS. I wonder why it has not been done?

Dr. GOWEN. Sir, I use the concept of today's technology. When you consider where we have been over the years, such equipment has been very expensive. But with the advent of microprocessors, and some of the new electronics that exist today there are things that can be done. One of the concerns here, sir, is that—and I guess when I speak in terms of regulations, there are pros and cons—clearly regulations that would have all equipment so manufactured tend to even out the cost of development, and we appreciate that in the marketplace. But fail-safe devices alone, if that is the concern, may not be cost effective. There is 5 to 10 percent retakes on films. Fail-safe concerns on films would take care of that percentage, maybe 2 or 3 percent of the X-rays used. That is a significant number when you consider the total amount. Our concern is looking at the cost of putting on a fail-safe as opposed to the greater training for the technologist who is already part of the system. Training may be a better use of funds as opposed to simply putting on more technology. I am not telling you here "Put on greater technology." Sure we can do it. But our concern is more directed at how we spend our tax dollars, yours and ours, as taxpayers.

Mr. ROGERS. Your concern is that the regulations may be discouraging technological development in this country?

Dr. GOWEN. Yes.

Mr. ROGERS. Particularly with X-ray? How is that exhibited?

Dr. GOWEN. It comes about like this: We are concerned about developing X-rays today that use very high technology, CT is perhaps the best example. The computed tomographic scanners which use much of the concepts and ideas that were developed for some of the deep-space probes, and they are very sophisticated machines. The development of those machines is expensive. This is a very rapidly changing technology. It has been in existence for 6 years. Within these 6 years we are already looking at a new vista, a new forefront, real-time scanning. A manufacturer would be a little reluctant to put an awful lot into the development of a new machine if the marketplace were going to change suddenly and you would not recover your investment. That is basically the way the marketplace looks now. If you further add the aspect of more regulatory change, you make the marketplace skittish. It is that point that I am addressing. There is a need for efficacious regulations but not needless regulations.

Mr. ROGERS. But may I say, too, I think you may find regulation has encouraged new development. I am not sure that it is as negative as you say. Now, I think we can be oppressive at times, but I must say I doubt if we would have much effort to reduce exposure levels unless there were some regulations to bring that about. What would be the incentive in the marketplace to reduce exposure levels? No reason. I do not see any incentive to do that. As a matter of fact, it might be better because you will have to come back and have more treatment.

So I must say I think often our regulations encourage new technology. The fact that we want to reduce exposure is encouraging ultrasound right now, the sonic area; that is coming about because of concern for radiation, so I think there may be a counterbalance here. I would agree with you, you can get too many regulations. But I think there may be untold examples of where regulations are bringing about improvements, as a matter of fact, even reductions in costs. The fact that we are now considering a cost containment bill has pretty much brought that CAT scanner down from $750,000 to where you can now buy them for less than $150,000. In fact, they now sell them even just a little above $100,000 because then their purchase would be exempt from review under the law. They would be able to sell as many of them as they want.

Now that has a positive effect on saving money for the American public. If we had set it at about 100, instead of 150, I expect they would be making them at about $90,000, because of the genius of our technology and the people who make it. So there is a counterbalance. I do not share the feeling that all regulation—you did not take that position—but we do often hear, "Oh, it is the regulations that are ruining everything."

That is not always true. I am sure you share some of that.

Dr. GOWEN. Sir, I am glad you recognize that we share that, because as an Institute you speak of our dollars, as they are yours. Let me give you an example on the other side. For instance, in the medical device regulations, we find for instance, a developer of a small catheter, a very special one, regulations caused the marketplace to be limited. The yearly gross was $15,000. The cost was $200,000 to try to meet the Federal regulations involved. Clearly the man could not afford the development and dropped it. It was not a broad market. Today there are a few CAT scanners, there are 500. But there are going to be many, many more. When we further develop the market, the price will become lower yet. It is a changing market. There will be new developments and as new developments come out, it is there——

Mr. ROGERS. I must say, the small producer has problems everywhere, it is not just because of a medical-device law.

Dr. GOWEN. That is correct.

Mr. ROGERS. We do not even have the old family grocer.

Dr. GOWEN. I am not speaking in terms of medical device laws only. I should make that clear. When I speak about regulations, I am not attacking any regulations of a group or this committee; it is a trend. There must be a balance. What we are calling for is there be an awareness in any regulations of the impact to be felt, that impact may be pro or con.

Mr. ROGERS. I think you called for voluntary certification.

Dr. GOWEN. Yes.

Mr. ROGERS. What is wrong with mandatory certification?

Dr. GOWEN. Well, mandatory certification or licensing exists in many areas, and clearly a barber, an engineer, a physician, a lawyer are all required to be licensed.

Mr. ROGERS. Engineers are not allowed voluntary certification.

Dr. GOWEN. Yes, sir, we have licensure, by every State in this Union.

Mr. ROGERS. Should we allow engineers voluntary certification?

Dr. GOWEN. Sir, I think, as you know from what I have given you in the testimony and our statement that we very much support the determination of competency for engineers.

Mr. ROGERS. You want to be sure that they are qualified and that the public may depend on that qualification. Now, should we also require that when people go to be X-rayed, they may depend on that operator knowing what he is doing, or should we just allow the operators to make that decision of whether they want to voluntarily be qualified or not?

Dr. GOWEN. Sir, there is a point that I would like to clarify.

Mr. ROGERS. All right.

Dr. GOWEN. What we have suggested in our statement, I would like to point out very clearly to you, is that we are calling for what we term engineering tradeoff studies in which we are asking to really look at what will be most effective. A balance between cost and effectiveness. We recognize that in calling for licensure of radiological technicians even with phased planning, would put a tremendous additional burden upon the health care system. The point we are raising is let's look at that burden. If that is effective, then do it. Perhaps if we go to certification and look at the question of the voluntary standard with incentives for following it——

Mr. ROGERS. If you are going to certify them, you are going to certify them. It is going to cost whether you do it the voluntary way or just require it. Whoever is going to have to teach them, or to administer the certification. I do not see the costs are going to be any different. How is the process going to have to be paid?

Dr. GOWEN. There is a question of the total cost to the system. It is possible to require certification. Ideally, I think it would be great to have everyone certified at the lowest cost as presented in our statement.

Mr. ROGERS. Here is the other cost factor, that when we talk about something as important as this, what is the cost factor to the public in health-damage if that operator is not qualified?

Dr. GOWEN. We agree. We agree very much, and share your great concern.

Mr. ROGERS. It is necessary for the safety of a building that an engineer is licensed, properly trained.

Dr. GOWEN. We are talking about a very great concern.

Mr. **Rogers**. I think I understand.

Dr. **Gowen**. I would like to make it very clear that we are calling for certification to establish better competency. Yet, I do not feel at this point in time we ought to conclude that licensure is necessary. We are calling for a tradeoff, study with a concern that we at least have certification.

Mr. **Rogers**. What are you trading it off with? I am not sure I understand that tradeoff when it involves the training of somebody who can affect the life of the person receiving that X-ray. I would think the tradeoff is either more cancer or less cancer vis-a-vis an unknowledgeable operator or the proper operator. I think that may be the tradeoff, rather than mandatory or voluntary certification.

Dr. **Gowen**. The tradeoff is not that one. I agree with you very much. The tradeoff I address is whether we as a health-oriented society are in a position to mandate the cost of licensure or whether we can achieve the same goal with incentives and voluntary certification. I do not address the question of whether licensure is good or bad.

Mr. **Rogers**. I do not think that with the States it would be too much of a problem. Anyhow, I think the points you have raised the committee will go into, and we are grateful for your being here and letting us have the benefit of your thinking. Perhaps we will be back to you.

Dr. **Gowen**. We very much would like the opportunity to assist your efforts, and we are very much appreciative of what you and the committee are doing. Thank you for the opportunity for being here.

[Testimony resumes on p. 1197.]

[Responses to questions submitted by the subcommittee follow:]

RESPONSES BY
THE INSTITUTE OF ELECTRICAL AND ELECTRONICS ENGINEERS
TO THE
SUBCOMMITTEE ON HEALTH AND THE ENVIRONMENT
QUESTIONS ON MEDICAL AND DENTAL DIAGNOSTIC X-RAYS

COMMITTEE (C) I RISKS TO HUMAN HEALTH

Several research studies have emerged in the last few years which suggest that the risk of adverse health effects resulting from exposure to low-level ionizing radiation is significantly greater than earlier research indicated. Several independent researchers, including Arthur Upton, Director of the National Cancer Institute, and Edward Radford, Chairman of the National Academy of Sciences' BEIR Committee, have told the Subcommittee that they agree with this conclusion.

Question 1 WHAT IS YOUR ASSESSMENT OF THESE NEW RESEARCH FINDINGS?

Answer 1:

Although the risk may be higher than initially thought, no direct evidence exists, but risk factors are extrapolated assuming a linear theory. The risk factors are probably not somatic but genetic in nature and if proven correct, could affect future generations. We recommend that more direct evidence at the pertinent x-ray practice parameters can be obtained to more knowledgeably assess risks.

Question 2 IF LOW-LEVEL IONIZING RADIATION PRESENTS A SIGNIFICANTLY GREATER HEALTH RISK, WHAT ARE THE IMPLICATIONS FOR THE MEDICAL AND DENTAL USE OF X-RAYS?

Answer 2:

It is imperative (if this is found to be the case) that the medical and dental users of ionizing radiations, the most frequent users of radiation in this country, apply only that amount of radiation to extract the information for the diagnosis.

A common practice in dentistry is to take a set of x-rays for all patients even if a current set is available. While such a practice is justified as ensuring a current patient profile, it does lead to the production of more x-ray exposure than might be required by the specific complaint.

Question 3 IF THESE FINDINGS ARE VALID, WOULD YOU RECOMMEND ANY CHANGES IN THE WAY DIAGNOSTIC X-RAYS ARE USED BY THE MEDICAL AND DENATL PROFESSIONAL? IF SO, PLEASE EXPLAIN.

Answer 3:

Better training and good equipment will be the most effective method of controlling patient and personnel expsores in diagnostic x-ray examinations.

In addition to those who build and those who operate x-ray equipment, continuing education is most essential for the radiologists and physicians who use the resultant images. Such education should include the extension of the practitioners knowledge of the benefit to cost trade off for the patient with each additional x-ray exposure. Support should be given to programs to develop educational packages to help acquaint radiologists with the potentials for greater use of the computed tomographic scanner.

There are various estimates of the number of x-ray images produced in excess of those required for a proper diagnosis. A recent study by the BRH (12) shows that from 5 to 10 percent of the x-rays must be retaken, largely due to technique and operator reasons. An additional unknown number of x-rays are taken to insure that every measure possible has been employed to make a thorough diagnosis in these times of increasing malpractice expense. Other x-rays are ordered to confirm a questionable diagnosis where more conservative treatment might negate the need for such x-rays.

An underlying consideration seems to be the low cost and convenience of a conventional x-ray. It is easy to see how one more x-ray requiring a few seconds of time and little materials could be considered as a high benefit payoff with only minimal cost. Such practicies assume that the cost of radiation exposure is largely negligible, but until pertinent data on the risks from low-levels of ionizing radiation are developed, this assumption may no longer be valid. Taking one film plate at a time, the radiation exposure could be negligible when compared with the benefits of a speedy diagnosis. However, when one considers the total aggregate expense, each additional x-ray must be closely evaluated to determine the patient benefit in comparison to the patient exposure risk.

We encourage radiological professionals to carefully consider modifying the current procedure of automatically ordering all views in a diagnostic series when it may be feasible to make a positive diagnosis with far fewer exposures. Such a procedure would expose the patient to the minimal number of x-radiations consistent with an adequate diagnosis, rather than simply apply a uniform examination schedule for all patients. Thus, as soon as a positive diagnosis is made, the patient would no longer be subjected to additional radiation exposure. If upon examination of such a survey film, a negative diagnosis is detected, then additional views could be taken to verify the negative diagnosis or arrive at a positive conclusion.

This "trade-off" approach makes many assumptions, ranging from the existence of a positive diagnosis x-ray view to the availability of adequately trained personnel to perform the procedure. Clearly, the all views for all persons approach is simple, even though it may produce redundant and thereby potentially needless information. This approach is optimized for the technicians and radiologists and not always the patient.

Also, x-ray procedures to "rule out" disease and the practice of obtaining studies at one time of the day with interpretation later in the day (or on the subsequent day) may required re-evaluation in consideration of minimizing patient radiation exposure rather than maximizing the efficiency of the x-ray department.

Question 4 THE FOOD AND DRUG ADMINISTRATION HAS ESTIMATED THAT 30% OF ALL DIAGNOSTIC X-RAY PROCEDURES ARE UNNECESSARY. DO YOU BELIEVE THIS ESTIMATE IS TOO HIGH, TOO LOW, OR ABOUT RIGHT? IF YOU DISAGREE WITH FDA, WHAT IS YOUR ESTIMATE?

Answer 4:

If the 30% figure includes excessive films due to the practice of all views for all patients, "retakes" due to technician error, examinations that do not contribute to the health management of the patient, or to faulty equipment, the figure may be correct or, indeed, a bit low.

Question 5 WHAT PERCENTAGE OF THE X-RAY PROCEDURES ADMINISTERED EACH YEAR IN THIS COUNTRY WOULD YOU ESTIMATE RESULT IN RADIATION EXPOSURE LEVELS WHICH ARE HIGHER THAN NECESSARY?

Answer 5:

The percentage of x-ray procedures performed by competently trained radiologists and radiologic technologists that result in higher than necessary patient exposure is small, probably in the range from 5-10%. However, the NEXT data developed by the Bureau of Radiological Health indicate that x-ray procedures performed by non-radiologists, result in a large percentage of higher than necessary patient exposures. For example, it was found that the average chiropractor uses an x-ray beam size 40% larger than necessary, the average general practitioner uses an x-ray beam some three times larger than necessary for chest x-rays, and a third of all dentists surveyed probably expose their patients to twice as much radiation as required for a satisfactory image. Most operators of diagnostic x-ray equipment do not know the level of radiation exposure patients are receiving in exams, except to tell the patient that "it's low and not to worry about it". Additionally, with 30 to 50 percent of the radiological technicicans presently functioning with little or no formal training in the proper techniques of minimizing patient exposure to radiation, we must conclude that at least one-fourth to one-third of all x-ray procedures result in higher than necessary patient exposure to extract the required diagnostic information.

Question 6 WHAT FACTORS OR INFLUENCES LEAD TO:
(A) UNNECESSARY X-RAYS?
(B) UNNECESSARILY HIGH RADIATION EXPOSURE?

Answer 6:

(A) UNNECESSARY X-RAYS?

Unnecessary x-rays, as discussed in the questions above, are a result of a number of factors:

1. Poorly or inadequately trained operators of radiologic equipment.
2. The practice of defensive medicine.
3. The practice of "all views for all patients" regardless of the symptomatology for medical and dental practitioners who are not specialized in radiology.
4. Retakes as a result of poor technique or faulty equipment.

(B) UNNECESSARILY HIGH RADIATION EXPOSURE?

Unnecessarily high patient radiation exposure is the result of:

1. Poorly or inadequately trained equipment operators.
2. Radiologic device operators who are inadequately trained in the dangers of excessive radiation to patients.
3. Faulty equipment.
4. X-ray over exposure coupled with film underdevelopment.
5. Ignorance of patient radiation exposure levels utilized.
6. Ignorance or confusion in patients concerning the dangers of radiation exposure.

Question 7 ARE THERE ANY INCENTIVES FOR A PHYSICIAN, DENTIST, CLINIC, HOSPITAL OR TECHNOLOGIST TO REDUCE THE EXPOSURE ADMINISTERED IN EACH X-RAY?

Answer 7:

At present, save the professional integrity of the radiological professionals, there are no effective incentives.

In the tradeoff or sensitivity study of the x-ray diagnostic system, it is clear that there is a high benefit to cost payoff (including the cost of unnecessary radiation exposure) if additional training and continued education is developed for the operators of diagnostic x-rays systems.

We recommend that a joint effort be initiated, with industry, the hospitals, the professional socieities, and the government joining forces to develop a training program reaching all corners of our country. The IEEE through its many member technical societies stands ready to assist in such a program. Ideally the implementation of such a health training service could be accomplished under the aegis of the state health agencies. The federal government, in cooperation with the third party payees, could provide an incentive for those hospitals, clinics, and radiological services that avail themselves of such training. The professional societies could assist in the preparation and continued updating of the materials. Potential delivery techniques range from the use of educational television, with the resultant secondary effect of an informed public (over 27 percent of the adult population is familiar with the characters used in daytime, school-aged, educational television), to home study audio-visual materials, conferences, and workshops.

In addition to providing an incentive system through payments to the care providers for encouraging these operators to participate in such training, a program of certification and recertification of competency is essential. While it is clear that the Federal government could legislate that such certification is required of all persons who operate radiological devices, it is equally clear that such legislative action would not receive enthusiastic support from radiation technologists and hospitals involved. Perhaps a more acceptable approach would be to provide for voluntary certification rather than mandatory licensing. Such certification could serve as a basis of fee authorization and payment to the health care providers. Such incentives might take the form of preferential third party and governmental payment schedules for organizations that continue to improve their diagnostic imaging services in a manner to promote better patient care along with reductions in the exposure to radiation and the cost per procedure.

Question 8 DO PHYSICIAN AND DENTIST EDUCATION PROGRAMS INCLUDE SUFFICIENT INFORMATION, TRAINING AND TESTING ON THE APPROPRIATE USE OF X-RAYS AND THE HEALTH RISKS ASSOCIATED WITH THE UNNECESSARY USE OF, OR OVEREXPOSURE TO, DIAGNOSTIC X-RAYS?

Answer 8:

The general practitioner and other non-radiologic physician specialities that perform routine radiographic examinations (such as orthopedic surgeons, etc.) include only sparse training in radiologic diagnosis. The basic principles of radiation and radiation protection training are found in a minute fraction of medical school curricula. More should be done, however, within most medical school curricula, no time slots are available for such training. Continuing education is most essential for the radiologists and physicians who use the resultant images. Such education should include the extension of the practitioners knowledge of the benefit to cost trade off for the patient with each additional x-ray exposure. Support should be given to programs to develop educational packages to help acquaint radiologists with the potentials for greater use of the computed tomographic scanner.

Such training programs are especially important as the radiologist moves from conventional techniques to those available with the computed tomographic scanners. Now is the time to provide for the development of educational packages for the transition from both conventional x-ray equipment and present scanners to realtime scanning techniques. The computed tomographic impact to date has represented a completed revolution in the procedures of how diagnostic imaging procedures are performed. The availability of realtime computed tomography promises an even greater revolution with even more efficient uses of x-rays to provide better diagnoses with dynamic studies.

Dentists receive somewhat greater exposure in their training to radiographic imaging and procedures involving the use of radiation but their training is lacking in the health related risks to x-ray overexposure. Frankly, this area is only now being recognized as an area of concern to the entire medical community where previously, only low health risk was associated with diagnostic radiologic procedures.

The IEEE supports and recommends passage of the Senate Bill S.2388 sponsored by Senators Packwood, Javits, and Nelson, and the House of Representatives Bill HR-111590 sponsored by Representative Steiger for the exclusion of employer educational assistance from the gross income of employees for tax purposes. Clearly, the passage of such legislation is vital to the development of effective educational program.

PROPOSED COMMITTEE FINDINGS

For the purpose of answering the following questions assume that as a result of these hearings Congress finds that:

(a) There is a reasonable probability that low-level ionizing radiation presents a more signifcant health risk than previously believed;

(b) The greatest portion of man-made ionizing radiation exposure to the public results from diganostic x-rays;

(c) A significant part of the medical and dental diagnostic radiation administered each year is unnecessary by reason of the x-ray itself being unnecessary, the procedure being poorly administered, or the equipment or material being defective or out of adjustment.

What recommendations do you have for reducing the incidence of unnecessary diagnostic x-rays? For instance would you recommend any of the following:

Question 9-- CHANGES IN THE MEDICAL EDUCATION SYSTEM?

Answer 9:

Several changes in the medical education system can have a significant impact on the reduction of patient radiation exposure. Introductory courses covering medical uses of radiation, their health risks and benefits and radiation protection for personnel and patients should be mandatory in the medical school curricula. It is true that not all medical students will pledge radiology as a speciality in their residency training but they will find themselves referring patients for radiologic procedures and in doing so, they should have at least rudimentary knowledge of the operating procedures of a radiology department that can be discussed with their patient as the primary care physician. If this is not accomplished and the assumed findings of this committee are valid, there could be instances (as has already been experienced in the "backlash" against mammography where women with breast symptoms are not being referred for x-ray examination) in which patients will not be referred for the x-ray procedure out of fear or ignorance.

In this same vein, the education of dentists, radiologists, and radiologic technologists should include more of the health risks associated with x-ray procedures. The Institute supports programs designed to produce informed public concerning these matters.

Question 10 -- CHANGES IN FINANCING OR REIMBURSEMENT FOR DIAGNOSTIC X-RAYS?

Answer 10:

We recommend a program of financial incentives be developed. Specifically, such a program of incentives be applicable to those who make improvements to reduce the exposure of patients to needless radiation. We recommend the immediate convening of a panel of knowledgeable experts from the areas of health care delivery, finance, government, and engineering to propose a program of incentives. We recommend that such a program of incentives be aimed toward rewarding those users of radiologic devices will reduce exposure of patients to radiation through improvements of radiologic equipment and radiologic techniques. We do not recommend that such necessary improvements be simply directed through legislative means but rather that the reimbursement and federal aid system be tailored to provide incentives for those who choose to improve their radiological services through training, certification, good practice, and responsive equipment improvement.

I encourage the committee to urge the cognizant federal agencies to convene a study panel with broad representation, including that of engineering and the x-ray research and development community, to establish reasonable goals and objectives for the continued improvement of x-ray equipment and procedures. Such a panel should also be charged with the development of incentives to encourage the improvement in both equipment and operational procedures. The IEEE is ready to support such a study panel. An important consideration in the formulation of such a panel is the assurance of knowledgeable engineering participation.

Such incentives might take the form of preferential third party and governmental payment schedules for health care organizations that continue to improve their diagnostic imaging services in a manner to promote better patient care with a reduction in patient exposure to radiation and the cost per procedure.

Question 11 -- GUIDELINES AS TO WHEN X-RAYS ARE AND ARE NOT APPROPRIATE?

Answer 11:

Guidleines have already been developed by the professional organization representing radiologists in several areas pinpointing when x-rays are and are not appropriate. For example, the x-ray procedure to determine whether an impending mother's pelvi structure was capable of allowing delivery of the term baby unharmed, called pelvimetry, was deemed unnecessary in most cases and recommendations were made against its routine use by these professional organizations. There are many other examples of guidelines such as this being published by the professional organizations representing radiologists across the country. We believe this approach to the development of guidelines by responsible professional practitioners is fundamental to the delivery of quality health care. We encourage the development of guidelines for good practice in the use of x-rays for diagnosis with particular emphasis on questionable or difficult diagnoses for which the absence of such guidelines encourages the physician to order a radiologic evaluation as protection against a future claim for damages because x-rays were not ordered. Additionally, we encourage radiological professionals to develop guidelines for new techniques for confirming diagnoses without simply reverting to the normal practice of exposing the patient to all views of a standard procedure when a more conservative approach as described in our statement to the committee, would result in a positive diagnosis with lower exposure of patients to needless radiation.

Question 12 -- GUIDELINES ON OPTIMUM EXPOSURE, FILM AND DEVELOPING TECHNIQUES?

Answer 12:

As indicated in our prepared statement, we strongly encourage the preparation of guidelines by responsible radiologic professionals. However, guidelines will not substitute for the adequate training of radiologic personnel. Unfortunately, guidelines all too often are used as substitutes for adequate training. A guideline only has meaning when it is used by a trained radiologic equipment operator. Maximum emphasis should be placed on the training of operators first and the development of guidelines for such trained operators. Secondly it would be a mistake to simply develop guidelines without providing adequate training for users of the equipment referred to by such guidelines.

Question 13 -- PUBLIC AND PATIENT EDUCATION AND INFORMATION PROGRAMS ON APPROPRIATE USE OF X-RAYS AND THE NEED TO AVOID UNNECESSARY EXPOSURES?

Answer 13:

In our prepared statement we strongly urge development of educational programs which will acquaint the American public with the dangers of needless exposure to radiation. We emphasize the training of practitioners and radiologic technicians. Such training can be provided through a multiplicity of delivering procedures including home study materials, conferences, workshops, and tutorial articles. In our statement we have emphasized the national system of public television in combination with those educational institutions offering educational television courses provides a unique opportunity for educating both the health delivery care professionals and the American public. As mentioned in our statement, public television is widely used in elementary and secondary school programs throughout the nation today. It has been found that over 27 percent of the adult population readily identify the characters of such children related television programs. Such public awareness of the dangers of ionizing radiation came through exposure to course material prepared for health care professionals and para-professionals would go a long way toward reducing the exposure of patients to ionizing radiation.

Question 14 -- ELIMINATION OF ROUTINE SCREENING PROGRAMS OR ROUTINE PRE-HOSPITAL ADMISSION X-RAYS?

Answer 14:

Each screening program should be evaluated for both its benefits, goals and associated risks. In this sense, routine screening programs, unless deemed "riskless", should be discouraged. Routine pre-hospital admission x-rays, with no indicated symptomatology indicated, should be discouraged. Special efforts should be made to modify the all views for all patients approach to screening and diagnosis.

Question 15 -- DEVELOPING A SYSTEM BY WHICH COPIES OF X-RAY FILMS COULD BE PROVIDED TO PATIENTS OR TO SUBSEQUENT PHYSICIANS OR DENTISTS?

Answer 15:

The pros and cons of providing copies of x-ray films, medical charts, etc., to patients or subsequent physicians or dentists have been debated and the issues are complex. However, as a means of lowering unnecessary radiation exposure, we support the practice of providing such copies of tests to patients, realizing that new examinations may be necessary in some cases. The old tests, however, could be beneficially used as baseline data for new studies.

Question 16 -- ARE THERE ALTERNATIVE DIAGNOSTIC PROCEDURES AVAILABLE WHICH ARE AS USEFUL OR MORE USEFUL THAN X-RAYS?

Answer 16:

In the January 1978 issue of the IEEE Spectrum, R. Jurgen reviewed the current status of ultrasound and other non-ionizing radiation diagnostic imaging modalities. The production of images through the use of ultrasound energy provides a means for statis and realtime visualization of internal organs. However at the present time, the image quality attainable is somewhat inferior to that obtained by x-rays. Additionally, the ultrasonic technique is highly dependent on the experience and capabilities of the operator for success.

Research must continue to sharpen the beam width, to better handle scattering from tissue interfaces, and to more clearly understand the changes introducing ultrasonic radiation into the tissues of the body. There is an easily developed theory that says that all external energy is destrimental to body tissues. Carried to the extreme, this theory would have us all placed in rooms where the temperature, sound level, electromagnetic environment, and even the atmospheric conditions are controlled. But more practically it seems apparent that there is a level around which our bodily systems can tolerate the introduction of certain energies without distrubing the functional equilibrium of the body tissue. The effects of ultrasonic energy are under evaluation and it appears that levels of energy normally associated with ultrasonic diagnostic equipment is below the level of the accepted tissue dosage threshold.

The attraction of thermography is that the measurement is made using inherent body energy and thus is a passive technique. Thermography has become a popular diagnotic tool for the evaluation of disorders that create surface localized hot regions. Thermography has been applied to the examination of the breast with mixed results.

Improvements in the techniques and instrumentation are essential if this procedure is to find adoption in diagnostic imaging. However, the passive thermographic technique has inherent limitations in the image resolution possible. First, the thermal energy produced by a disorder must be conducted to the surface of the skin in a manner that will facilitate identification of the disorder. Additionally, the sensitivity of the detectors must be further improved to more clearly delineate the outline of the disorder under study.

A major attraction of the thermographic techniques is their inherent suitability to programs of mass screening. With additional research and development they may reach that desired goal.

Technologies are evolving to produce diagnostic images using ultrasound and thermographic techniques. While useful in many types of diagnosis today, considerable research and development is necessary before the technology will be advanced to the point of significantly replacing ionizing radiation as a diagnostic imaging technique. Research and development funds are essential.

Question 17 -- TO WHAT EXTENT DOES MALFUNCTIONING EQUIPMENT, POORLY ADJUSTED EQUIPMENT, CONTRIBUTE TO THE INCIDENCE OF UNNECESSARY DIAGNOSTIC X-RAYS (FOR INSTANCE, REQUIRING "RETAKES")?

Answer 17:

In a study published in 1975, the "retake" rate due to all causes was estimated at 5-6% at two large hospitals. Other studies have estimated the retake rate as high as 10%, again from all causes, malfunctioning equipment being only one of the parameters affecting "retakes". It may be estimated that only 1-2% of the retakes could be attributed to faulty or poorly adjusted equipment. By equipment one should include not only the radiographic unit but the automatic film processor also, since the greatest cause of "retakes" in virtually all of the studies was rooted in incorrect film density or contrast.

Question 18 -- WOULD IMPROVEMENTS IN EQUIPMENT DESIGN REDUCE THIS PROBLEM?

Answer 18:

Yes, definitely. However, even though technology exists to perform diagnostic radiology with all encompassing safeguards, the cost of this approach must be analyzed and balanced against the returns achieved with better operator training coupled with a more informed public.

I urge this committee to recommend the adoption of acautious posture, a questioning posture, an evaluative posture concerning the promulgation of additional regulations that could stiffle the development of new equipment and procedures providing better health care delivery. I encourage the committee to call for a careful evaluation of the impact of the 1974 and 1976 diagnostic radiation device and medical device regulations. Not only the impact in dollars, but the real impact in delivering the most efficacious care to the patient. I encourage to the committee to call for the appointment of a "blue ribbon" panel of engineersand medical scientists to evaluate the costs and benefits of all proposed and existing health device regulations. There is an urgent need for an independent panel to make what we in engineering call, a "trade-off" study, which is an indepth evaluation of the impact of proposed changes. The use of such a "trade-off" or sensitivity study is simply a systematic means of exploring and evaluating all realistic approaches to the solution of a particular problem. We use such analyses whenever it is essential to optimize the impact of possible decisions. Our members support the need to optimzie our limited resources in combination with a need to reduce the radiation exposure to the patient. Such a "blue ribbon" panel can serve a vital purpose in the integration and evaluation of the many comments, suggestions, and evidence presented concerning the impact of proposed regulations in the application of technology to better health care.

There is need for more research and development in the technology used in the production of x-ray images. Greater sensitivity in sensors will help advance the potential for reducing even further the dose of x-rays associated with a computed tomographic scan. It is particularly important that the federal agencies be readily aware of their important role in the continued development of health care technologies such as that found in the computed tomographic scanner. The competition for the survival of a company in such a high technology area is intense. It is difficult for a company to recover the costs of each technological development when it is forced to continually develop its produce line or lose out in the market place.

Federal assistance in the development of improvements in the computed tomographic scanners could be helpful, if not essential, particularly if it were given with adequate patent and investment protection.

In addition to the continued development of the computed tomographic scanner technology leading to realtime scans, it is imporatant to carefully consider incentives for the continued improvement of conventional x-ray technology. The technology exists today to control x-ray techniques and x-ray emissions so that each patient receives only the minimal amount of radiation to produce the image needed for a diagnosis. Techniques exist to ensure the operation and calibration of the x-ray machine prior to the emsission of energy to the patient. Quality control methods are available to maintain film processing quality and thus minimize the need for retakes due to poor development procedures. We do not advocate regulating these improvements, but rather that the reimbursement and federal aid system be tailored to provide incentives for those who choose to improve their radiological services through training, certification, good practice, and responsive equipment improvement.

Question 19 -- WHO SHOULD BE RESPONSIBLE FOR ASSURING IMPROVEMENTS IN EQUIPMENT DESIGN?

Answer 19:

The IEEE is dedicated to excellence in engineering and science and supports programs to recognize and reward proven comptency. This is particularly the case in the practice of engineering that has a direct impact on the public, such as in the development of health care technology. It is the policy of the IEEE to encourage the licensure and registration of engineers as professional engineers when they are responsibly involved in products that have an impact on the public. I ask that this committee join in supporting our goal that at least a minimal level of competency be assured in the design, assembly, and evaluation of x-ray equipment through the proper employment of professional engineers for positions requiring the exercise of engineering approval of equipment that will have a direct interface with patients such as x-ray equipment. Input from professional organizations to the manufacturers of daignostic radiologic equipment should be supported and furthered. Coupled with the equipment improvement incentives mentioned previously, federal agencies could effectively assure that these improvements are incorporated into the equipment used in diagnostic radiology.

Question 20 -- TO WHAT EXTENT DO TECHNICAL OR TECHNICIANS ERRORS CONTRIBUTE TO INCREASING THE NUMBER OF X-RAYS TAKEN?

Answer 20:

While it is difficult to quantify how many needless x-rays are taken, there is not doubt that technician errors contribute to increasing the number of x-rays taken. Although many safeguards have been incorporated into equipment function and design to obtain consistent quality radiographs, it is still the person to machine interface in the final analysis that affects the quality of radiographs. The fact that many x-ray departments continue to use untrained or minimally trained technicians certainly contribute to unnecessary patient exposure. In our statement, we have strongly recommended that programs of education be initated immediately.

Question 21 --WHAT CAN BE DONE TO MINIMIZE SUCH ERRORS?

Answer 21:

Educational programs are the most effective way to minimize such errors. Many radiologic technologist programs are designed to take a high school candidate and with a two year or less training program turn out an individual who has the prime responsibility for producing diagnostic quality imagery at the lower possible patient exposure. Much of the training is the "on the job" variety and student technologists are frequently found as the only technologist working in a diagnostic room due to economic rational. This practice should be discouraged.

We are concerned that approximately half of the 130,000 operators of radiologic equipment in the United States have received appropriate formal training. This situation is of further concern because, as stated by Mr. C. Hardin, representing the Conference of Radiation Control Program Directors before the Senate Committee on Commerce, Science, and Transportation in 1977 (11),

> ". . . I would like to express another concern of the states which has also been expressed at the federal level. Specifically, as reported in the Bureau of Radiological Health staff report entitled "Diagnostic Medical X-ray Technologiest: The Issue of Qualifications," dated January 19, 1975: "With the exception of 13,000 radiologists, who are expert in the use of radiation for diagnostic and therapeutic purposes, physicians are generally not trained in the principles and practices of radiation protection, and what radiologic training the non-radiologists physician does receive, either in medical school courses or during the clerkship or internship periods, is almost entirely concerned with part of physicians' training, and this is particularly significant in view of the fact that the performance of the examination is largely delegated by physicians to more than 100,000 X-ray machine operators, many of whom do not possess formal credentials certifying their

competence. The situation in many instances, then, is that of a supervisor untrained in radiation protection directing an equally untrained employee."

As mentioned in the previous question, we strongly urge a program of education be started immediately and we are ready to assist in such an endevor.

Question 22 --WOULD BETTER SELECTION AND TRAINING OF TECHNICIANS HELP MINIMIZE SUCH ERRORS?

Answer 22

It is essential to provide the most competent technicians available if the health care delivery is to be maintained. It is especially important that a competency of such technicians be periodically evaluated and such persons be motivated to continually improve their level of expertise-if a reduction of exposure to patients needless radiation is to be achieved. In our statement we recommend a program of voluntary certification with fee incentives provided to those health care delivery organizations who employ only technicians whose competency has been verified by a strong program of certification.

Question 23 --WHO SHOULD BE RESPONSIBLE FOR POOR PERFORMANCE OF TECHNICIANS?

Answer 23

The physician who orders the use of an x-ray should be responsible for the safe performance of the technician in producing such an x-ray. A patients physician as the primary care provider and as such, must assume the responsibility for the provision of effacious and effective care including diagnostic x-ray procedures. Such monitoring of the performance of technicians is a complex question. In many cases it is unreasonable to expect the physician to be present for all x-ray procedures. However it is only placed in the hands of trained, competent technicians.

Question 24 -- WHAT IS THE RESPONSIBILITY OF THE RADIOLOGIST OR OTHER PHYSICIAN IN MONITORING TECHNICIAN PERFORMANCE?

Answer 24

Please refer to our answer to question 23.

Question 25 -- WHAT RECOMMENDATIONS DO YOU HAVE FOR REDUCING THE AMOUNT OR EXPOSURE USED EACH TIME AN X-RAY IS TAKEN?

Answer 25

We encourage the radiological professionals to carefully consider modifying the current procedure of automatically ordering all views in a diagnostic series when it may be feasible to make a positive diagnosis with far fewer exposures. Such a procedure would expose the patient to the minimal number of x-radiations consistent with an adequate diagnosis, rather than simply apply a uniform examination schedule for all patients. Thus, as soon as a positive diagnosis is made, the patient would no longer be subjected to additional radiation exposure. If upon examination of such a survey film, a negative diagnosis is detected then additional views could be taken to verify the negative diagnosis or arrive at a positive conclusion.

This "trade-off" approach makes many assumptions, ranging from existence of a positive diagnosis x-ray view to the availability of adequately trained personnel to perform the procedure. Clearly, the all views for all persons approach is simple, even though it may produce redundant and thereby potentially needless information.

Question 26 -- ARE THERE IMPROVEMENTS IN EQUIPMENT OR MATERIALS DESIGN WHICH WOULD REDUCE THE LEVEL OF EXPOSURE PER FILM?

Answer 26

More sensitive film-screen systems, image intensifying phosphors, and other image receptor systems are being developed and introduced by industry to the diagnostic radiologic community at an ever increasing pace. More effective information transfer routes between the engineering and scientifically based research personnel, industrial developers and the medical community should be encouraged to allow further, more efficient adoption of these equipments and materials. Lower dose systems with requisite diagnostic information transfer characteristics should obtain disbursal aid to the radiologic community from the professional organizations.

Question 27 --WHO SHOULD BE RESPONSIBLE FOR ASSURING SUCH IMPROVEMENTS IN EQUIPMENT DESIGN?

Answer 27

Providing for improvement in equipment design is a complex problem. In some instances equipment design improvements can be achieved through regulations issued in response to legislation. In other instances equipment improvements can be discouraged by additional regulations. We propose that a panel of experts be convened to carefully evaluate the effectiveness of regulations in providing for improvements in radiologic equipment design. We have also proposed that a second panel of experts be convened to develop incentives, perhaps in the form of a differential fee reimbursement schedule from governmental third party payees, to encourage improvements in both equipment and practice which will lead to reductions in exposure to radiation. Ideally such panels could be convened under the direction of the Bureau of Radiologic Health. The final assurance that improvements are made at the local level should be the responsibility of state radiation control organization. It is also essential that funding be provided to enable these state agencies to carry-out such a mandate. It is our recommendation that a minimum of regulations, incentives and inspections may be the best way to achieve the needed improvements in patient exposure. Such a mix appears to also have the advantage that it can be accomplished at the lowest overall cost.

Question 28 -- ARE THERE ADEQUATE SCIENTIFICALLY-BASED PROFESSIONAL GUIDELINES FOR THE APPROPRIATE USE OF DIAGNOSTIC X-RAYS?

Answer 28

In general, yes. These guidelines originate from professional organizations such as the ACR, federal agencies such as the BRH, and are recommended to the radiologic community. Their acceptance is voluntary in many cases, however.

Question 29 -- WHAT STEPS COULD BE TAKEN TO DEVELOP AND IMPLEMENT SUCH SCIENTIFICALLY-BASED, PROFESSIONAL GUIDELINES?

Answer 29

We believe the American College of Radiology should be the clearing house for such guidelines regarding the practice of radiology. Input from all segments of the scientific research and industrial R&D community relative to equipment design and improvements in diagnostic health care delivery should be evaluated by the panel recommended in our statement, and passed on to the ACR for its evaluation and dissemination to its members.

Question 30 -- IN YOUR JUDGEMENT WHAT WOULD BE THE BEST MECHANISM FOR REQUIRING, APPLYING AND MONITORING THE APPLICATION OF GUIDELINES SO THAT BOTH THE FREQUENCY OF UNNECESSARY X-RAYS AND THE LEVEL OF RADIATION EXPOSURE DUE TO DIAGNOSTIC USE CAN BE REDUCED?

Answer 30

Again, the recommendations of the ACR should be the best mechanism of assuring the recommended guidelines of "good practice" on the local level, the Joint

Commission on Accreditation of Hospitals, in conjunction with field representatives of the federal agencies responsible could monitor on a hospital to hospital basis the incorporation of these guidelines. Incentives provided by third party reimbursers would aid in incorporation of the guidelines in diagnostic radiological practice.

We have made several specific suggestions in the answers to questions above and we strongly urge that those recommendations be implemented.

Question 31 -- IF YOU BELIEVE THERE IS A ROLE FOR THE FEDERAL GOVERNMENT TO PLAY IN REDUCING UNNECESSARY DIAGNOSTIC X-RAYS AND THE TOTAL RADIATION DOSE RECEIVED FROM DIAGNOSTIC RADIATION, PLEASE OUTLINE THE IMPORTANT ELEMENTS OF THE APPROPRIATE FEDERAL ROLE?

Answer 31

We recommend that the federal government assume a role in reducing unnecessary exposure to radiation through the following actions:

1. Convene a panel of engineers, medical scientists and health care providers to develop a program of incentives to reward those users of radiologic equipment who modify their radiologic procedures and equipment to minimize the exposure of patients to diagnostic radiation.
2. Develop an awareness program for practitioners and technicians using radiologic equipment which will educate these care providers in the dangers and causes of excessive exposure of patients to diagnostic radiation.
3. Encourage the development of improvements in existing equipment by convening a panel of health care providers and financial and engineering experts to evaluate the effectiveness of federal medical device and radiological equipment regulations in reducing the risks to patients from needless exposure to radiation. In particular, we recommend that the panel focus on a cost to benefit study to identify the most effective approach for regulations. The present process of agency review does not include, as a significant part of the evaluation procedure, a consideration of whether a specific regulation approach is the most effecacious way to achieve the desired protection of patients.
4. Encourage the evaluation of radiological procedures to minimize the amount of exposure to ionizing radiation for a specific diagnosis.
5. Encourage the development of alternative diagnostic imaging techniques which do not require ionizing radiation.

Mr. ROGERS. We are grateful for your presence.

The last witness is Robert G. McCune, who is division manager, Radiation Imaging Products Division, National Electrical Manufacturers Associations, Washington, D.C.

We welcome you to the committee, Mr. McCune. We are anxious to have your statement. It will be made a part of the record in full. And if you could highlight the major items, the committee would appreciate it.

STATEMENT OF ROBERT G. McCUNE, DIVISION STAFF MANAGER, RADIOLOGICAL IMAGING PRODUCTS DIVISION, NATIONAL ELECTRICAL MANUFACTURERS ASSOCIATION

Mr. McCUNE. We do have a formal statement [see p. 1201], as you stated, and I will only cover the major points of our statement.

Mr. McCUNE. I now have an abbreviated version of my abbreviated version. And if you will permit a personal observation here before proceeding I would like to say I have noted some of the other witnesses who have paid tribute to the chairman. And I too am experiencing a feeling of sadness as I appear in front of this committee because of the knowledge this will undoubtedly be my last time to appear before you, Mr. Chairman. For myself and the National Electrical Manufacturers Association, as members of the regulated health care industry, we want to thank you on the record for your many years of dedication and contributions to improving the American way of life, and wish you great success in your new career.

Mr. ROGERS. Thank you for your very fine remarks.

Mr. McCUNE. I am here today as the representative of the radiological imaging products industry. This industry trade group represents 57 companies who manufacture radiological products used in the practice of diagnostic medicine—conventional medical and dental X-ray, computed tomography, diagnostic ultrasound, nuclear and therapy.

At the request of the subcommittee staff, I earlier furnished a written industry statement dealing with increased radiological equipment cost. In the cost data previously submitted and also attached to this statement you will note that the annual percentage of increases for X-ray equipment is below or consistent with the wholesale industrial price index except for 1974 and 1975. The higher increases in those 2 years resulted from the implementation of the Radiation Control For Health and Safety Act of 1968 and the removal of wage and price controls. I am prepared to discuss further this cost information as you desire.

But the principal purpose for my appearance here today is to discuss this industry's point of view on other issues that we understand are of concern to the subcommittee which we, as equipment manufacturers of radiological technology, can appropriately address.

We believe the mission of diagnostic imaging equipment manufacturers is to enhance health care through the development and supply of products and services for diagnosis, treatment planning, and therapy which will enable the medical profession to provide improved and cost-effective patient care. At the same time, the industry expects to provide its employees improved opportunities and to provide its owners with an adequate return on invested capital.

Toward these ends, there has developed during the past 27 years a symbiotic relationship between the medical profession and the medical equipment manufacturers. Without the physicians, we in industry would not understand health care needs, and without the industry, physicians would lack the tools which are so necessary in the practice of their profession.

The ability to treat disease depends on the ability to make a diagnosis, and today diagnosis is heavily dependent on the ability to create images of body organs or of tumors or of other diseased tissues. In the absence of exploratory surgery, these body organs are hidden from view, and so resort is made to various techniques such as X-ray, ultrasound, or nuclear tracers to produce the images from which a diagnosis can be made.

The free enterprise system has some inefficiencies and limitations, to be sure, and those of us who work in it are well aware of them. However, it is also a very effective method of preventing impractical, marginal, or unrealistic devices from coming to the marketplace, or if they should appear in the marketplace, to weed them out.

It is reasonable, then, to conclude that because the price structure of the medical equipment manufacturing industry has been able to include the necessary research and development expense, valuable diagnostic imaging devices have come forth. The devices have and continue to permit diagnosis and treatment planning of a quality that is difficult to envision being obtained otherwise.

While the purchase cost of a high technology diagnostic imaging equipment system can range into the hundreds of thousands of dollars, it is most important to recognize that the usable life of an imaging system can be managed to last for many years and will continue to provide its original performance quality.

We believe a serious question to be addressed by legislators is, what will the impact of current legislation be on the development of new technology to meet current and future demand for improved medical diagnostic information? Obviously, such development is an expensive undertaking with considerable commercial risk. It would even become less attractive to an independent manufacturer if the marketplace was to be controlled as a result of government legislation. Such legislation may secondarily affect whether new technology applied to medical diagnostic information is to be limited and also how needed development may be funded.

When one considers the role of medical equipment in the process of identifying and diagnosing health problems, through to curing of the patient, it is apparent that equipment advances can have tremendous leverage on the total health care cost. And when we realize that the yearly purchase of diagnostic imaging equipment represents only about 0.6 percent of the total health care dollar, it is obvious that any savings in the remaining 99.4 percent could easily exceed any extra cost in diagnostic imaging equipment. Suppose our industry had done no R. & D. for the last 10 years, except for cost improvement programs. It is true that medical equipment would be less expensive, but let's see what the effect might have been on the total health care system.

One: Possibly twice as many women would be dying before age 50 of breast cancer, undetected until it has become so large metastasis would invariably have occurred. Mammography would be available but with lower resolution and at dose rates so high that it would be used only in serious cases, often too late. The opportunity for useful mammography at relatively low doses would still be a dream.

Two: There would be no widely available way to measure the pumping capacity of the heart, or of actually seeing the area of myocardial infarction. The knowledge required to do constructive heart bypass operations would not be available, resolution of overlapping arteries would be very difficult.

Three: CT would not exist. We would have no way to see brain tumors, only to infer their presence. The number of painful, risky pneumoencephalograms and angiograms would have only increased, and not been replaced by the less traumatic outpatient procedure now available.

Four: Today's ultrasound imaging, especially useful in examinations where X-radiation is undesirable, would similarly not exist. Visualization of a heart valve motion, especially important in determining if replacement of the valve is required, would still be a dream.

One cannot calculate the increase in the other 99-plus percent of the health care expenditures that would be required to offset a reduction in equipment spending, because no amount of money would have provided the same diagnostic information from the equipment available 10 years ago. In fact, we would be spending more for less, with tumors discovered only when they were larger and more likely to cause death, heart bypass surgery essentially impractical, more people in hospitals to die rather than be cured and for more money, not less.

Better diagnosis, with less patient trauma, increasingly on an outpatient basis, with more reliable productive equipment. That's what results from research and development spent on diagnostic equipment.

Admittedly, costs are rising, and health care costs are no exception. However, laying the blame at the base of technology is both illogical and fiscally shortsighted. The initial costs of new technology are high in some cases, but the day-to-day application and use of technology pays dividends in actual dollars and cents of increased efficiency and productivity.

Of equal importance, technology pays tremendous social benefits. New technologies replace older, less effective, and more costly tests and procedures. New diagnostic technologies are capable of detecting abnormalities earlier and more efficiently than ever before. New technologies improve the manner in which health care is delivered to individuals and society as a whole.

Put another way, the probable effect of overly restrictive legislation and regulation would be to deny a large segment of the population access to major effective diagnostic service; to perpetuate less efficient diagnostic practices which contribute to prolonged inpatient care and delayed recovery; to continue to support surgical intervention for purposes of exploration and diagnosis; and to discourage research and development of new technologies.

Optimal use of any new technology depends on the accessibility of the technique and the opportunity to explore its full potential. Artificial limitations on the use of a new technology, on the other hand, serve only to institutionalize outmoded procedures and inefficient practice.

The social and economic environment today requires that we take full advantage of all the clinical and cost-saving potential that medical technology has to offer. The future demands that we embrace all of the developing advances in medical technology that science makes possible.

Thank you.

[Testimony resumes on p. 1219.]

[Mr. McCune's prepared statement and attachment follow:]

STATEMENT OF ROBERT G. McCUNE

Mr. Chairman and Members of the Subcommittee:

My name is Robert G. McCune, and I am the Division Staff Manager for the Radiological Imaging Products Division of the National Electrical Manufacturers Association*.

I appreciate the opportunity to appear before the Subcommittee on Health and the Environment during these important oversight hearings.

I am here today as the representative of the radiological imaging products industry. This industry trade group represents fifty-seven companies who manufacture radiological products used in the practice of diagnostic medicine (conventional medical and dental X-ray, computed tomography, diagnostic ultrasound, nuclear and therapy.)

At the request of the Subcommittee Staff, I earlier furnished a written industry statement dealing with increased radiological equipment cost. In the cost data previously submitted and also attached to this statement you will note that the annual percentage of increases for X-ray equipment is below or consistent with the wholesale industrial price index except for 1974 and 1975. The higher increases in those two years resulted from the implementation of the Radiation Control For Health and Safety Act of 1968 and the removal of wage and price controls. I am prepared to discuss further this cost information as you desire.

But the principal purpose for my appearance here today is to discuss this industry's point of view on other issues that we understand are of concern to the Subcommittee which we, as equipment manufacturers of radiological technology, can appropriately address.

---

*NEMA is the principal national trade association of the electrical manufacturing industry. The Association has some 550 member manufacturing companies, which are affiliated with one or more of its product Divisions, each Division representing in essence a separate and distinct industry. The electrical products within NEMA's scope are used either as components or as end-equipment in all major phases of the generation, transmission, distribution, control and utilization of electrical energy.

We believe the mission of diagnostic imaging equipment manufacturers is to enhance health care through the development and supply of products and services for diagnosis, treatment planning, and therapy which will enable the medical profession to provide improved and cost-effective patient care. At the same time, the industry expects to provide its employees improved opportunities and to provide its owners with an adequate return on invested capital. Toward these ends, there has developed during the past seventy-five years a symbiotic relationship between the medical profession and the medical equipment manufacturers. Without the physicians, we in industry would not understand health care needs, and without the industry, physicians would lack the tools which are so necessary in the practice of their profession.

The ability to treat disease depends on the ability to make a diagnosis, and today diagnosis is heavily dependent on the ability to create images of body organs or of tumors or of other diseased tissues. In the absence of exploratory surgery, these body organs are hidden from view, and so resort is made to various techniques such as X-ray, ultrasound, or nuclear tracers to produce the images from which a diagnosis can be made.

The history of diagnostic imaging began with the discovery of X-rays by Roentgen in 1895. Within a year, X-rays were being employed for medical purposes and an industry as well as a new medical specialty -- radiology -- began to grow. The research and development was funded by industry with risk capital. By World War I, field X-ray equipment was already available to save lives in the battle areas. By 1920, industry had developed the double-emulsion X-ray film, and in the 1920's William Coolidge developed the hot cathode X-ray tube. These developments, funded by industry, made radiology a practical, clinical method of diagnosis which quickly spread throughout the world. In 1937, an X-ray machine with the capability of doing both fluoroscopy and radiography with film was introduced, and during World War II some 10,000 portable units of this type were supplied to the military on every battle front. The resultant improvement in the care and treatment of the wounded was of incalculable value.

Another major milestone in the improvement of health care through diagnostic imaging came in the early 1950's with the invention of the image intensifier tube, generally credited to John Coltman. Previously, fluoroscopic images had been very dim, obscure pictures visible only to the dark adapted eye. With the image intensifier, bright images could be produced with low X-ray exposure.

It further became possible to make X-ray movies -- cine radiography -- to visualize moving organs and to follow the course of opaque materials injected into the blood stream. Heart surgery, such as the coronary bypass operation, then became possible with the resultant saving of many lives and the improvement in the quality of life for many more.

Another important development was the specialized chest X-ray unit, which made possible mass screening of high risk populations for tuberculosis. These machines have now been developed to the point where they include automatic film handling and film processing, so that mass production techniques are possible in the hospital. The machines require considerable capital investment by the hospitals, but as is commonly the case, the capital investment reduces hospital labor and improves cost effectiveness. With the aid of these machines, tuberculosis has been largely wiped out in the United States.

About six years ago, computed tomography -- the CT Scanner -- was developed. The CT Scanner employs both sophisticated X-ray technology and the modern computer to produce images which look like slices taken out of the head or body of the patient. Earlier X-ray pictures always showed all of the bones and body organs superimposed on one another, and were difficult to interpret. The earlier X-rays also failed to distinguish in many cases between healthy and diseased tissue.

The CT Scanner overcomes these difficulties, and consequently has been in great demand. Because of its high initial cost, the CT Scanner has become very controversial in an economy dedicated to control of health care expenses. Nevertheless, the unique ability of CT images, not only to show the existence of disease but to portray with new precision its

its nature and extent, is having significant impact on the subsequent course of treatment of patients. It permits medical resources to be applied to patients in the most helpful ways, and it avoids unnecessary surgery and its associated costs and trauma.

Other diagnostic imaging modalities follow a similar path of development. There have been occasional developments achieved with government money, but the vast majority of research and development efforts have been funded by private industry. In nuclear medicine, early work was done at Oak Ridge National Laboratory, but the enormous benefits of nuclear medicine could never have been realized without the private development of the rectilinear scanner, which makes a picture or map showing the location of trace amounts of radioactive material in the body. For the first time, this permitted physicians to easily locate cancer tumors in patients' bodies. Then a camera was developed which could do the job faster and could therefore trace the movement of radioactive material in the body. Industry, after the investment of many millions, converted it into a practical clinical tool which is now the very heart of nuclear medicine. Diagnosis of many bone diseases, cardiac diseases, glandular disorders, and the like, are now possible and it seems clear that nuclear equipment will continue to play a major role in the diagnosis of disease and understanding of dynamic body functions and body physiology.

A similar case can be made in the development of ultrasonic methods for imaging and diagnosis. The basic principles of ultrasound were developed originally under the auspices of the Navy, which used Sonar very effectively in searching for hostile submarines. However, it was not until a private company undertook to provide a physician with a specialized ultrasound unit that the application to medical diagnosis was understood.

The value of ultrasound as a noninvasive method of imaging can hardly be overstated. As one example, the development of ultrasound has progressed to the point where many diseases of heart valves can be diagnosed simply and quickly without subjecting the patient to the trauma and risks associated with heart catheterization.

The value of ultrasound in the soft tissue region of the abdomen is also enormous. The fact that it is noninvasive and nonionizing gives it great potential as a screening tool in many, many areas. It is of great value in the medical care and planning with difficult pregnancies.

Most of the scientific apparatus which I have described was developed in industrial research laboratories with private financing. There has always been considerable risk in making these investments, but the risk was acceptable in an environment where a definite contribution to the improvement of health care would be rewarded with a fair return on the investment.

The free enterprise system has some inefficiencies and limitations, to be sure, and those of us who work in it are well aware of them. However, it is also a very effective method of preventing impractical, marginal, or unrealistic devices from coming to the marketplace, or if they should appear in the marketplace, to weed them out.

It is reasonable then, to conclude that because the price structure of the medical equipment manufacturing industry has been able to include the necessary research and development expense, valuable diagnostic imaging devices have come forth. The devices have and continue to permit diagnosis and treatment planning of a quality that is difficult to envision being obtained otherwise.

While the purchase cost of a high technology diagnostic imaging equipment system can range into the hundreds of thousands of dollars, it is most important to recognize that the usable life of an imaging system can be managed to last for many years and will continue to provide its original performance quality.

We believe a serious question to be addressed by legislators is, what will the impact of current legislation be on the development of new technology to meet current and future demand for improved medical diagnostic information? Obviously, such development is an expensive undertaking with considerable commercial risk. It would even become less attractive to an independent manufacturer if the marketplace was to be controlled as a result of Government legislation. Such legislation may secondarily affect whether new technology applied to medical diagnostic information is to be limited and also how needed development may be funded.

In the medical equipment industry, investments in research and development often exceed, sometimes by a substantial margin, the gross profits of the business. Nevertheless, continued investment in this research and development results in better health care. Each manufacturer invests to maintain his share of the business. They compete aggressively against each other, and the company that can develop better products, sell their value at a lower price, provide better training and service, succeeds. History is replete with companies who did not make the required investment and are no longer in this business. This is free enterprise at its finest, and our society has benefited from this competition.

Let me give you some specifics. In the mid-fifties, one company developed an automatic X-ray film processor, that eliminated the need for hand-dipping of X-ray film by technicians, and at the same time improved the average quality of the films produced. This saved labor costs, X-ray exposure to patients due to fewer retakes, and improved the patient throughput of diagnostic X-ray systems. The introduction of this automatic processor in 1957 resulted in a surge of buying, but has given cost savings ever since to the health care system.

In recent years, X-ray generators that operate more reliably, with finer control over exposure, sometimes powering X-ray tubes in more than one room, were introduced. You can say that companies had to develop these new models to be competitive, and that is true. But the health care system was the benefactor, saving money and time through more effective equipment, because of our competitively-inspired engineering.

Incidentally, much of this engineering is directed at what we actually call "cost improvement." This effort has permitted the industry to hold price increases to a minimum, even a rapidly inflating economy. For example, the simple single phase X-ray generator that was introduced in the late 1950's, is available today for about the same price in dollars. It is important to note that higher prices for certain equipment, say the new three-phase X-ray generator, relates to a much better performing, more reliable machine than was available at any price in the late 1950's.

Research and development is also used to develop new areas, to open new markets, to provide diagnostic equipment that can detect problems earlier, with more confidence than before. Here research and development is more risky, because we frequently won't know how successful it will be until we have done much of the work and spent most of the money. Let me describe these examples.

In the last three years, several X-ray companies have developed specialized vascular X-ray equipment that permits for the first time visualization of the left anterior descending coronary artery. Being able to resolve overlapping arteries in this area of the heart is critical to sound cardiac diagnoses. The decisions regarding heart surgery can now be made with better information, the result of R & D on X-ray equipment made in close cooperation with the medical profession.

In another area, the last seven years have seen tremendous improvements made in mobile X-ray generators. Many of these units are powered using rechargeable batteries. This eliminates the need for special heavy duty circuits to supply high amperage current throughout the hospital, and by using a drive motor to power the machine, moving of the heavy unit is made much easier for radiologic technicians. Once at the bedside, the high quality of the X-ray generator reduces the need for retakes or repeat exposures, saving technician time and radiation to the patient. While this X-ray generator is primarily aimed at the patient too sick or immobile to move to the Radiology Department, it turns out that the unit also does yeoman duty during emergencies and power outages. Today no hospital would want to be without at least one mobile unit.

Sometimes R & D is not so successful. For example, in the late 1960's infra-red scanning or thermography appeared to be an attractive, noninvasive, nonradioactive method of breast cancer screening. Initial medical tests were encouraging. The government included thermography in many of its 27 breast screening centers. Selected companies invested money in this modality--in sales and service organizations, in training physicians--all with the expectation that the investment would generate some return. Unfortunately, in this particular case the follow-on results were not favorable. Better ways to use X-rays, including Xeroradiography and low-dose film systems, were developed, and with time, the clinical results from thermography were found to be less definitive. Physicians simply stopped calling for thermography tests and machine sales stopped. In fact, manufacturers and distributors were stuck with many machines in inventory, with the probability that the research and development invested here will never pay off.

However, we tend to be optimists or we wouldn't be in this business, so we continue searching and accept the kind of risk manufacturers in the medical equipment area make every day, with the knowledge and expectation that (1) when we succeed, we invariably improve our total health care delivery system; and (2) that the medical professionals will make the determination as to our success in an atmosphere free of unusual restrictions.

When one considers the role of medical equipment in the process of identifying and diagnosing health problems, through to curing of the patient, it is apparent that equipment advances can have tremendous leverage on the total health care cost. And when we realize that the yearly purchase of diagnostic imaging equipment represents only about 0.6% of the total health care dollar, it's obvious that any savings in the remaining 99.4% could easily exceed any extra cost in diagnostic imaging equipment. Suppose our industry had done no R & D for the last ten years, except for cost improvement programs. It's true that medical equipment would be less expensive, but let's see what the effect might have been on the total health care system.

1. Possibly twice as many women would be dying before age 50 of breast cancer, undetected until it had become so large metastasis would invariably have occurred. Mammography would be available but with lower resolution and at dose rates so high that it would be used only in serious cases, often too late. The opportunity for useful mammography at relatively low doses would still be a dream.
2. There would be no widely available way to measure the pumping capacity of the heart, or of actually seeing the area of myocardial infarction. The knowledge required to do constructive heart by-pass operations would not be available, resolution of overlapping arteries would be very difficult.
3. CT would not exist. We would have no way to see brain tumors, only to infer their presence. The

number of painful, risky pneumoencephalograms and angiograms would have only increased, and not been replaced by the less traumatic outpatient procedure now available.

4. Today's ultrasound imaging, especially useful in examinations where X-radiation is very undesirable, would similarly not exist. Visualization of a heart valve motion, especially important in determining if replacement of the valve is required, would still be a dream.

One can't calculate the increase in the other 99+% of the health care expenditures that would be required to offset a reduction in equipment spending, because no amount of money would have provided the same diagnostic information from the equipment available ten years ago. In fact, we would be spending more for less, with tumors discovered only when they were larger and more likely to cause death, heart by-pass surgery essentially impractical, more people in hospitals to die rather than be cured and for more money, not less.

Better diagnosis, with less patient trauma, increasingly on an outpatient basis, with more reliable productive equipment. That's what results from research and development spent on diagnostic equipment.

The common goal we share is to deliver high quality health care to all of the American people at a cost that society can bear. We share the belief that an orderly and rational course of action is needed in order to reach that goal. We believe that advanced medical technologies are the most potent tools we have to keep costs under control, while providing significant social benefits as well. If we limit the availability of technically advanced medical modalities, the effect will be to encourage more labor intensive procedures, and total health care costs will actually increase. Furthermore, society may well be deprived of a wide range of benefits it would otherwise receive unless a more orderly course of technological utilization is provided.

BEST COPY AVAILABLE

Technology has added significantly to mankind's longer life expentancy. As recently as 125 years ago, 131 out of every 100,000 infants died at birth in this country. The life expectancy for the general population was a short and brutish 38 years. But as other new medical technologies were introduced, such as Pasteur's experiments with bacteria in 1862 which led to the germ theory of disease, Lister's antiseptic techniques for surgery in 1865, and when the diagnostic arts were given a powerful new tool in 1895 with the discovery of X-rays, life expectancy increased significantly.

To diminish technological research and development at this time would be to permit children to continue to perish from brain tumors, osteopathic sarcoma, leukemia, congenital heart disease and carcinoma, and to let people continue to die from heart attacks and cancer at the peak of their lives and careers. It may not be possible to quantify future effects of technological advances on life expectancy, but it is safe to predict setbacks in the fight against disease and disability if technology and research are discouraged by misdirected limitations.

Admittedly, costs are rising, and health care costs are no exception. However, laying the blame at the base of technology is both illogical and fiscally shortsighted. The initial costs of new technology are high in some cases, but the day-to-day application and use of technology pays dividends in actual dollars and cents of increased efficiency and productivity.

Of equal importance, technology pays tremendous social benefits. New technologies replace older, less effective, and more costly tests and procedures. New diagnostic technologies are capable of detecting abnormalities earlier and more efficiently than ever before. New technologies improve the manner in which health care is delivered to individuals and society as a whole.

Put another way, the probable effect of overly restrictive legislation and regulation would be to deny a large segment of the population access to major effective diagnostic service; to perpetuate less efficient diagnostic practices which contribute to prolonged inpatient care and delayed recovery; to continue to support surgical intervention for purposes of exploration and diagnosis; and to discourage research and development of new technologies.

Optimal use of any new technology depends on the accessibility of the technique and the opportunity to explore its full potential. Artificial limitations on the use of a new technology, on the other hand, serve only to institutionalize outmoded procedures and inefficient practice.

The social and economic environment today requires that we take full advantage of all the clinical and cost-saving potential that medical technology has to offer. The future demands that we embrace all of the developing advances in medical technology that science makes possible.

Thank you.

RADIATION IMAGING PRODUCTS DIVISION

National Electrical Manufacturers Association
2101 L Street, N.W.
Washington, D.C. 20037 • (202) 457-8400

July 6, 1978

The Honorable Paul G. Rogers
Chairman, Subcommittee on Health
and the Environment
Interstate and Foreign Commerce
Committee
U. S. House of Representatives
Washington, D. C. 20515

Dear Mr. Rogers:

On May 11, 1978, the Radiological Imaging Products Division, National Electrical Manufacturers Association (NEMA)*, was contacted by the House Interstate and Foreign Commerce Subcommittee on Health and the Environment Staff and requested to submit an industry statement dealing with increased radiological equipment cost over the past five years. It was made known to us that the requested information would be considered during planned oversight hearings to be conducted by your Subcommittee on the health effects of low-level ionizing radiation, and additionally, the attendant cost factors of the purchase of diagnostic equipment, utilization rates of such equipment, and the impact of regulatory actions on the cost of manufacturing.

As an industry trade group, the Radiological Imaging Products Division of NEMA represents fifty-seven companies who manufacture medical radiological products used in the practice of diagnostic medicine (conventional medical and dental X-ray, computed tomography, diagnostic ultrasound, nuclear and therapy). Therefore, we agreed to undertake to prepare the requested information with the understanding that the statistical data collected and available to NEMA was by necessity limited in terms of type and purpose of data collected.

For example, NEMA members do report dollar figures for total X-ray equipment orders received on a monthly basis. These figures are reported as lump sum figures, however, and

---

*NEMA is the principal national trade association of the electrical manufacturing industry. The Association has some 550 member manufacturing companies, which are affiliated with one or more of its product Divisions, each Division representing in essence a separate and distinct industry. The electrical products within NEMA's scope are used either as components or as end-equipment in all major phases of the generation, transmission, distribution, control and utilization of electrical energy.

BEST COPY AVAILABLE

not by type of X-ray unit or system. In trying to identify a unit price increase element in X-ray equipment a problem exists in that X-ray units or systems cover an extremely broad price range from, for example, a simple portable generator system to an expensive, complex vascular system.

NEMA members do report data on unit orders received for many of the major components of complete systems. NEMA has attempted to utilize this data along with the total dollar orders data to generate an index showing an annual price increase for a "standard X-ray system unit." This "standard X-ray system unit" has been created by using a weighting factor based on the relative prices of the various X-ray systems. For example, a vascular system has a price approximately 62 times the price of a portable generator or, in other words, a vascular system is defined to contain 62 "standard system units" where a portable generator is defined to be one "standard system unit."

A summary of the index thus generated is attached hereto as Exhibit A for the time period 1974 through 1977 inclusive. 1974 has been used as the base year because previous to that time data was not collected by NEMA on total X-ray equipment orders received. A partial data base was generated in 1973 but NEMA has little confidence in the validity of the data due to start-up problems associated with data collection.

The data set forth in Exhibit A shows that the index has increased from a base of 100 in 1974 to a value of 130.6 in 1977 showing an average annual increase of 9.3 percent. These increases are compared to other Department of Commerce generated indices on Exhibit B. This exhibit shows that the X-ray equipment index increased at a lower annual percent rate than the medical care (includes hospital services) index, the hospital service charges index, the miscellaneous electrical equipment index, and the U. S. Wholesale Industrial Index. This data also shows that in the 1976 and 1977 time periods the X-ray index increased at approximately the same rate as the Consumer Price Index published by the Department of Commerce. The rate of increase in these years for the X-ray equipment index was 6.0 and 6.7 percent, respectively.

It should be pointed out that the X-ray equipment industries' costs are probably best represented by the U. S. Wholesale Industrial Index and the Miscellaneous Electrical Equipment Index, each of which increased at a higher rate than the NEMA X-ray equipment price index in this time frame.

Also, in the 1974 time frame the X-ray equipment industry was implementing performance standards issued by the FDA's Bureau of Radiological Health. These performance standards required redesign of many products and increased the costs of such products by a significant amount. These costs are undoubtedly reflected in the fact that the largest annual increase of the NEMA X-ray equipment price index of 15.5 percent occurred in the 1974-1975 time period. In addition, increased energy, labor and material expenditures, and higher product liability insurance premiums also contributed to increased costs for X-ray equipment manufacturers.

In summary, we believe the enclosed data shows that the price of X-ray equipment systems in the 1974 through 1977 time frame increased at a lower rate than X-ray equipment manufacturer's costs and at a lower rate than that of similar products being offered by industry. We believe that the information presented herewith is responsive to the questions posed by members of the Subcommittee Staff. However, we stand ready to offer any assistance to facilitate your review and comprehension of the data in advance of the oversight hearings. We are also prepared to comment further on the data at the time of our scheduled testimony.

Thank you.

Sincerely,

Robert G. McCune
Division Staff Manager

RGM:ev
Enclosures A & B

EXHIBIT A

Column	A	B	C	D	E
Year	NEMA X-Ray Equipment Orders (Millions $)	"Standard X-ray System Units" Ordered	Price of "Standard X-ray System Unit" ($)	NEMA X-ray Equipment Price Index	% Price Increase From Previous Year
1974	440.9	113242	4335	100	
1975	417.2	83321	5007	115.5	15.5
1976	450.7	84913	5308	122.4	6.0
1977	499.1	88150	5662	130.6	6.7

EXHIBIT A METHODOLOGY

NEMA EQUIPMENT VALUE INDEX 1974 - 1977

Each of the following items is reported by NEMA members in terms of the number of unit orders received on a periodic basis. Sales price data is not reported by NEMA members for individual items or systems, but total dollar value of orders received for x-ray equipment are reported to NEMA (column A).

In order to calculate an x-ray equipment cost index a weighting factor, which is a relative indication of the price of each system, has been applied to each of the systems actually reported as unit orders as follows:

	System		Weighting Factor
	Portables		1*
	Mobile radiographic		3
	Stored energy & capacitor discharge		4
	Mammographic		7
	Fluoroscopic/image intensifier		10
**	Conventional radiographic (all)	table	11
	Automatic chest units		12
**	Special purpose - tomographic	table	26
**	R & F Tilt (except remote control	"	30
**	R & F Tilt (remote controlled)	"	34
**	Special purpose - vascular		62

* Estimated average value index for portable system used as a base unit.

** Tables are major components and the assumption is made that they are generally a key equipment factor in the assembly of an X-ray system.

The weighting factor is multiplied by the actual number of units reported as orders. A number representing the total number of "systems" ordered each year is then obtained by summing all of the multiplied numbers (Column B).

The unit price (Column C) was developed by dividing the dollar value of equipment orders received (Column A) by the number of weighted unit orders (Column B). 1974 was used as the base year as it is the first year in which complete data was submitted on all x-ray equipment orders.

EXHIBIT B

PRICE INDEXES - 1974 BASE

Year	X-Ray Equipment (1)	Medical Care (Includes Hospital Services) (2)	Hospital Service Charges (2)	Misc. Electric Equipment (2)	U.S. Wholesale Industrial (2)	Consumers (2)
1974	100	100	100	100	100	100
1975	115.5	112	114.8	120.3	111.5	109.1
1976	122.4	122.5	129.3	129.3	118.5	115.4
1977	130.6	134.5	142.6	135.7	132.2	122.8
Ave. Annual Rate of Increase	9.3%	10.4%	12.6%	10.7%	9.8%	7.1%

Sources: (1) NEMA Data
(2) US Dept. of Commerce

Mr. ROGERS. Thank you very much for a very helpful statement. I think the question of research and development is an important one, and I think R. & D. is encouraged and should be. Of course it is true we should make sure the technology is used properly, for instance, that X-ray is not used on women under 50 because not only does it not prevent the disease but in many cases we have testimony today it causes cancer. So new technology, of course, has to be used properly and sometimes it takes a while to know.

Where would you say the major pressure for technological advances in safety and lower radiation comes from?

Dr. MCCUNE. Self-survival in the marketplace. I have documented in the full statement a number of advancements in radiology since the invention some 85 years ago, and many of those, or most of the major ones, were done prior to any regulation. Obviously we have the greatest incentive in a very competitive market to produce the most efficient and safest equipment possible.

We have a purchaser by normal product marketing that is tremendously intelligent, knows the product, is very selective, and knows safety. And so when we deal with that kind of customer we must do the best we can.

Mr. ROGERS. You do not think any rules or regulations are necessary?

Mr. MCCUNE. I think here is always a benefit from some regulation. I am not sure I would agree with you, Mr. Chairman, that it is the major motivation that has created many of the safety improvements. Obviously, when you have that kind of regulation you take steps. You mentioned failsafe. We added failsafe into the basic operating components before the act. As a result of that regulation, we took other steps to be sure that our equipment would be better in terms of operating more continually in a safe manner by improved failsafes. In other words, we gave to the system, backup systems that would insure, hopefully, the opportunity to avoid a recall or notice of defect.

Mr. ROGERS. What happens when efficiency and cost take you in one direction and safety in another?

Mr. MCCUNE. I am sorry.

Mr. ROGERS. What does the marketplace say when efficiencies and cost take you in one direction and safety takes you in the other?

Mr. MCCUNE. To the best of my knowledge, safety has never been an economic consideration in the marketplace.

Mr. ROGERS. May I say if you look at the automobile industry, I think we have had too much movement in many areas and there has to be some requirement for safety and regulation.

Mr. MCCUNE. That is a good example, Mr. Chairman, but in the manufacture of radiological equipment the manufacture is conducted by engineers and physicists who recognize that danger.

Mr. ROGERS. Except for instances where failures in some of the equipment brought about the first radiation health and safety act. Some of the equipment was leaking.

Mr. MCCUNE. Leaking?

Mr. ROGERS. Radiation. Then we got into television, and microwaves. I doubt if much would have been done if there had not been the act.

Mr. McCune. I do not want to leave the impression that we do not respect the regulation; in fact, our own voluntary standard for X-ray equipment was the basis on which the regulatory performance standard was considered and we had that standard on the books for some time. I can only say to you that we have learned to be good citizens with that regulation and support it.

Mr. Rogers. I was glad to see in your testimony the movement toward ultrasound so that we can accomplish results that are now brought about by radiation.

Mr. McCune. Yes, sir. We are spending millions of dollars in perfecting it. But let me tell you that modality is already coming under fire from critics who do not understand the modality, do not believe that it is totally safe, just because there are no reported incidents of injury. And we are beginning to get a little sensitive in that respect, as we did on CT scanners. People question whether there isn't some potential danger lurking in the background. I am glad to see the committee's consideration of diagnostic ultrasound.

Mr. Rogers. I presume you are funding some health effects studies?

Mr. McCune. Yes, sir. We have had epidemiological studies underway for several years. We have encouraged the FDA and others to do more. We are working with such groups as the American Association of Physicists in Medicine, we have joint committees, we are exchanging information. In fact in diagnostic ultrasound, even though there is not yet a medical device regulation we have spent a year and a half getting a voluntary standard prepared so that we can offer it to the Bureau of Medical Devices, and the same with nuclear cameras. We have not been sitting back waiting for someone to tell us to do something.

Mr. Rogers. I commend you for that.

Do you have any government contracts in this field?

Mr. McCune. Not as private manufacturers.

Mr. Rogers. In the research?

Mr. McCune. No, sir.

Mr. Rogers. I know we are doing some.

Mr. McCune. They are doing it within the Bureau of Radiological Health and we commend them. We just do not want the jury going out before all the evidence is in.

Mr. Rogers. Nor do we want to hang people before they are tried, so I think probably we see eye to eye.

Mr. McCune. Absolutely.

Mr. Rogers. Hopefully, a proper meshing of regulation and research and development in the private sector can bring about better safety, better technology for the public.

Mr. McCune. We would like to keep working at that.

Mr. Rogers. Thank you for your presence today. Your testimony is most helpful.

I believe this concludes the hearing, and the subcommittee stands adjourned.

[The following statements and letter were received for the record:]

STATEMENT OF
SISTER AGNES THERESE DUFFY, R. T., PRESIDENT
AMERICAN SOCIETY OF RADIOLOGIC TECHNOLOGISTS
BEFORE THE
SUBCOMMITTEE ON HEALTH AND THE ENVIRONMENT
OF THE
HOUSE COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE
OVERSIGHT HEARINGS ON RADIATION HEALTH EFFECTS
OF MEDICAL AND DENTAL DIAGNOSTIC X-RAYS
JULY 26, 1978

Mr. Chairman, Members of the Committee, my name is Sister Agnes Therese Duffy. As President of the American Society of Radiologic Technologists and on behalf of the membership, I am pleased to present this statement for the Committee's consideration in these oversight hearings on radiation health effects of low levels of ionizing radiation. We commend the Committee for its attention to this very timely subject.

Inasmuch as other experts have testified about the risks of medical radiation, my remarks will address what I consider to be the source of the problem -- the operator of the machine that produces that radiation.

Radiation is unique. It cannot be detected by any of the senses. Yet its use can save lives; its abuse can damage or destroy life. Any and all radiation emitted by properly calibrated equipment is produced solely by the action of the operator.

The operator of the equipment performs all functions necessary for the production of a radiograph, including the exposure of the patient to the radiation. Consequently, it is the qualifications of the operator, not those of the physician, which determine both the quality of the radiologic service and the radiation dosage to the patient. Because of the inherent danger of radiation, The American Society of Radiologic Technologists believes that every patient, and I repeat, every patient, deserves a qualified operator.

From its inception, our Society has recognized that formal education coupled with moral obligation has been a controlling factor in the competence of the individual and in the reduction of unnecessary radiation to both the patient and the operator. The safe and efficacious use of medical X-ray equipment should not and cannot be learned by hit-or-miss, on-the-job methods.

A Bureau of Radiologic Health staff report, "Diagnostic Medical X-Ray Technologists: The Issue of Qualification" dated January 1975 states: "Data from FDA/State Surveys, . . . the HEW sponsored proficiency text for X-ray technologists, and results from voluntary registration examinations demonstrate that knowledge and performance of credentialed technologists is better than that of non-credentialed personnel."

There are an estimated 130,000 to 170,000 operators of medical X-ray equipment in the United States. Of these, approximately 80,000 have demonstrated their competence through voluntary certification of state licensing examination. The remaining 50,000 to 90,000 have no recognized credentials.

To be more specific, in Florida, an estimated 45% of the operators are not credentialed by any authority. In North Carolina and Alabama, about half of the operators fall into this category. And in Kentucky, approximately 55% of the operators exposing the patient to medical radiation have never established any evidence of formal education in the use of this diagnostic tool.

In fact, only three states -- New York, New Jersey, and California -- now require operators of medical X-ray equipment to demonstrate their competence. Kentucky, Arizona, and Florida will require credentials this year. A few other states have passed enabling legislation, but have not yet developed the necessary regulations to license operators. In all other states, anyone -- absolutely anyone -- can expose the patient to radiation.

Since 1967, with introduction of the Radiation Health and Safety Act (now Public Law 90-602), The American Society of Radiologic Technologists has supported the enactment of Federal minimum standards of education and training for operators of medical radiation equipment. It has and will continue to support Federal legislation giving impetus to State licensure based on national standards, preferably the standards espoused by The American Registry of Radiologic Technologists, a national voluntary certification agency.

While we support national standards we recognize the necessity for state regulation to provide assurance of adherence to those standards. This very concept of national standards for qualification of educational programs and radiological personnel to serve as a model for states is embraced within legislation introduced in the Congress earlier this month, on July 13, 1978, by the Honorable Jennings Randolph, (D.-W.Va.), entitled "The Consumer-Patient Radiation Health and Safety Act of 1978". This bill, S. 3290, while embodying the rights of all Consumer/Patients encourages state adoption of national standards for the qualifications of educational programs and the personnel that provide radiological health care services. Further it promotes utilization of the voluntary system in implementing those standards. In addition to the states with licensure acts, accredited programs for education of radiologic technologists already exist on a voluntary basis in every state. The United States Office of Education recognizes the Committee on Allied Health Education and Accreditation, in cooperation with the Joint Review Committees, as the accrediting agency. These programs are also sanctioned by the respective professional organizations.

I might point out that if the American Registry of Radiologic Technologists, a National Voluntary Certifying Body, is deemed to fit the requisite of the law more than 80,000 of the estimated 130,000 - 170,000 operators of ionizing radiation equipment could automatically be grandfathered into the proper category of diagnostic X-ray (radiography), nuclear medicine, or radiation therapy. Let me reiterate, these 80,000 individuals have voluntarily prescribed to educational standards and testing for certification as a commitment to patient care and radiation protection.

But what about the 50,000 to 90,000 operators without credentials? For those technicians not certified by the American Registry of Radiologic Technologists we feel that continuing education coupled with the proficiency examination resultant from Public Law 92-603 can readily serve as a tool of measurement and a prerequisite for licensure. The urgent need for legislative action to reduce unnecessary exposure to medical radiation is brought sharply into focus by the following excerpts from a statement given by a Registered Nurse who, although instrumental in patient care, has never received training in radiological services. She stated:

> "For two years I worked for four Doctors in a clinic in the metropolitan area. The new knowledge of X-ray was passed on to me by seven other co-workers, (2 RN's, I LPN, 2 Lab Techs, 2 Medical Assistants). It didn't take me long to sense that taking X-rays was NOT easy. Fear for myself, the patient, and the respect I have always had for radiation was again present. I see X-ray as unique, the machines are complex and have to be thoroughly understood inside and out before using them properly. Besides the machine, the patient is the most important. They are paying and expecting that the best quality diagnostic results will be produced by the person taking the films.
>
> "I remember many repeat films having to be done by every employee, resulting in more X-ray exposure than necessary for the patient. My quick training was from the other personnel who had no formal X-ray training, we just learned what we could from each other. I personally felt pressure not only in using X-ray equipment, but coming up with good enough results acceptable to the Doctor, who would many times give me

> the benefit of the doubt even if the film was not the best. I couldn't help but wonder -- did he miss the diagnosis? What about the patient? X-rays were only read by a Radiologist in case of an obvious finding. Other areas of safety that weren't utilized were proper or consistent shielding of patients, coning, or the use of a radiation monitoring system for employees."

Similar situations exist around the country. A limited study performed in 1966 by the Bureau of Radiologic Health in 8 states and the District of Columbia showed that among part-time machine operators, approximately 13% were listed occupationally as "secretary or other" and that 94% had no X-ray training at all.

The American Society remains firm in its opinion that without uniform national standards for qualifications of medical radiation technologists, the public health will remain unprotected from untrained personnel.

We are not alone in our stand that competency of the individual is paramount in good radiological health care services and that national standards for qualifications are desirable . . . and needed. State government agencies share in our concern. During its 6th annual meeting, the National Conference of Radiation Control Program Directors (an organization of State and Local Radiological Health personnel) passed a resolution urging Congress to adopt legislation to require that persons administering diagnostic X-ray be adequately trained and experienced to assure efficacious use of X-ray equipment for the protection of the public health and maximum benefits to the patients. The Health Physics Society and The American Public Health Association have taken similar stances for national standards in an effort to promote uniform application among states.

We were encouraged last year to note that the Public Health Service report entitled, "Credentialing Health Manpower," released in July, 1977, addressed this issue in its Recommendation 11, which stated:

> "National standards for the credentialing of selected health occupations should be developed and continually evaluated. Professional organizations, other elements in the private sector, and State governments should play a significant role in this process. The standards thus developed should be utilized for the various purposes for which standards are required, including professional certification, licensure, private sector and civil service employment, and third party reimbursement."

Earlier this year the President of the United States determined that the time had come for action. On January 26, 1978, he signed Executive Order No. 10831 which approved a number of recommendations for the guidance of Federal Agencies. Recommendation Number 8 stated:

> "Operation of medical or dental X-ray equipment should be by individuals who have demonstrated proficiency to produce diagnostic quality radiographs with the minimum of exposure required; such proficiency should be assessed through national performance-oriented evaluation procedures or by didactic training and practical experience identical to, equivalent to, or greater than training programs and examination requirements of recognized credentialing organizations."

This recommendation had previously been agreed to and endorsed by the Administrator of the Environmental Protection Agency and the Secretary of Health, Education and Welfare.

The ASRT believes that the higher standard of radiation protection in the diagnostic use of X-ray that will ultimately be provided to the patients treated at Federal Agencies should be extended to all patients who must be exposed to medical radiation. We believe that Senator Randolph's new approach is sound and that it responds to the legitimate reservations of those who have been reluctant to support legislative efforts to provide for Federal licensure.

Mr. Chairman, the American Society of Radiologic Technologists held its 50th Annual Meeting at Anaheim, California, from July 14th to July 21st, 1978. After considering S. 3290, the new legislation sponsored by Senator Randolph, the Society adopted a resolution urging the enactment of S. 3290 by the United States Congress. A copy of that resolution is attached to this statement and we ask that it be included in the record. For reference purposes a copy of S. 3290, introduced in the United States Senate on July 13, 1978, by Senator Jennings Randolph (D.-W.Va.), and a Section by Section Summary are also attached and we request that both be printed in the Record.

We commend this Committee, Mr. Chairman, for its very proper and timely concern with respect to the radiation health effects of medical and dental diagnostic X-rays and, as we feel this whole legislative area is one needing urgent attention, we urge the Committee to continue its efforts to seek sound legislative solutions and, in particular, to direct its careful consideration to S. 3290 which we believe is essential to protect the American public from the potential hazards of radiation.

RESOLUTION IN SUPPORT OF S. 3290

WHEREAS, since 1968 the American Society of Radiologic Technologists, a National Professional Organization of Radiologic Technologists has gone on record in support of the enactment of Federal minimum standards in education and training in Radiologic Technology as a means of protecting the United States Public from exposure to unnecessary radiation; and

WHEREAS, the Society believes that unnecessary radiation exposure constitutes a hazard of national import to the public health; and

WHEREAS, the President of the United States has recognized the need for high quality radiological service in all Federal installations and has endeavored to insure this by promulgating Executive Order 10831 approved January 26, 1978; and

WHEREAS, the principle of radiation protection through competency of operators has been recognized by fifteen State legislatures as essential for consumer protection; and

WHEREAS, it is essential to maintain a high level of quality within State programs, there is a need for Federal technical and financial assistance to the States; and

WHEREAS, the Society is convened at Anaheim, California, July 14-21, 1978, and regards it appropriate to express deep concern with respect to the unnecessary radiation exposure of patients caused by inadequately educated and trained individuals; and

WHEREAS, the Society is advised that legislation was introduced in the United States Senate on July 13, 1978, designated as "The Radiation Health and Safety Act of 1978", by the Honorable Jennings Randolph (D. W.Va.) which is formulated to provide for the establishment of criteria and guidelines for the credentialing or licensure of all personnel administering radiation to consumer-patients and the accrediting of programs for the education of radiologic technologists and to encourage the States to adopt and administer such programs; and

WHEREAS, the Society has supported this concept in legislature as introduced into the 90th through 95th Congress, now therefore,

BE IT RESOLVED: That the American Society of Radiologic Technologists expresses its support of S. 3290, as sponsored by Honorable Jennings Randolph, United States Senator from West Virginia, which addresses the protection of the public from the hazards of radiation and by adoption of this resolution urges its enactment by the United States Congress.

BEST COPY AVAILABLE

SECTION BY SECTION

S. 3290, The Consumer-Patient Radiation Health and Safety Act of 1978

PART I - GENERAL PROVISIONS

Section 101 - The short title is the "Consumer-Patient Radiation Health and Safety Act of 1978".

Section 102 - This section sets forth the Congressional finding that it is in the interest of the nation's public health and safety to minimize exposure of consumer-patients to potentially hazardous radiation from radiologic procedures. Additional findings are set forth including in Section 102(e) that the protection of the public health and safety from unnecessary exposure to potentially hazardous radiation from such radiologic procedures is the primary responsibility of State and local government.

Section 103 - The purposes of the Act are to provide for the establishment of criteria for the credentialing or licensure of all personnel administering radiation to consumer-patients and for the establishment of similar criteria and guidelines for programs training such personnel. In addition, a purpose is to insure all Federal agencies administer programs to further the purposes of this Act.

Section 104 - Definitions are set forth in this section including (1) "medical practitioners" as licensable doctors of medicine, osteopathy, or chiropractic, who do or will prescribe or administer radiation to consumer-patients or for specified limited procedures, postgraduate physician trainees, such as interns and residents, and (2) "radiologic technologist" as any person, other than a medical or dental practitioner, who administers radiation to consumer-patients and includes, but is not limited to, medical radiologic technologists (including radiographers), dental radiologic technologists (including dental hygenists and dental assistants), radiation therapy technologists, and nuclear medicine technologists.

PART II - FEDERAL RADIATION PROTECTION GUIDELINES

Section 121 - The Administrator of the Environmental Protection Agency is directed pursuant to existing law to promulgate Federal radiation protection guidelines with respect to medical and dental radiologic procedures. Such guidelines are to be promulgated within 18 months of enactment for (1) the application of diagnostic X-rays to consumer-patients; (2) the therapeutic application of radiation to consumer-patients; and (3) the application of radiation to consumer-patients in the treatment of disease, such as nuclear medicine applications.

PART III - ESTABLISHMENT OF STATE PROGRAMS FOR THE CONTROL OF RADIOLOGIC SERVICES

Section 131 - The Secretary of Health, Education and Welfare is directed, by December 31, 1980, to issue voluntary standards for the accreditation of educational institutions conducting programs in radiologic services. The Secretary is authorized to certify appropriate professional organizations, such as those recognized by the Commissioner of Education, to certify such accreditation.

Section 132 - The Secretary of Health, Education and Welfare is directed, by December 31, 1980, to issue voluntary standards for the licensure of radiologic technologists. Such standards may distinguish between categories of specialization or levels of competence for the purpose of licensure.

In addition, the Secretary, within one year after issuance of such voluntary standards, is directed to review and evaluate any existing voluntary certification programs or State licensure programs to determine whether such programs meet such standards.

Section 133 - The Secretary is directed to provide advice and assistance to the States as necessary to foster establishment of appropriate programs to achieve the purposes of this Act. Such assistance shall include model laws.

Section 134 - The Secretary is authorized to make grants to educational programs accreditated pursuant to Section 131.

Section 135 - The Secretary is authorized to make grants to State and professional organizations designated pursuant to Section 131 for the planning, development, and establishment of programs to carry out the purposes of this Act. Such grants may be up to two-thirds of the first year's cost and up to one-third of the second, third, and fourth year's costs for such programs.

Section 136 - The Secretary is authorized to make 50 percent program grants to State radiation protection agencies to carry out the purposes of this Act. Such grants are conditioned on State adoption of the criteria and minimum standards for the accreditation of educational programs and for the licensure of radiologic technologists.

PART IV - FEDERAL ACTIVITIES

Section 141 requires that Federal agencies comply with the minimum standards promulgated pursuant to this Act.

Section 142 directs that the President, within one year of enactment, issue an Executive Order to require that Federal financial assistance be conditioned on the adoption of the miminum standards promulgated pursuant to this Act.

PART V - ADMINISTRATION

Section 151 requires that any guidelines and standards be prescribed in accordance with 5 U.S.C. 553. The Secretary is directed to consult with the Environmental Protection Agency, State health departments, and appropriate professional organizations.

PART VI - APPROPRIATIONS AUTHORIZATION

Section 161 authorizes such appropriations as necessary to carry out the purposes of this Act.

TESTIMONY SUBMITTED TO HOUSE SUBCOMMITTEE ON HEALTH AND THE ENVIRONMENT BY E. DEL SMITH ON BEHALF OF XONICS INCORPORATED: AUGUST 1, 1978

Xonics Incorporated is pleased to submit testimony to the Subcommittee On Health and The Environment with regard to development of technology to reduce exposure in medical radiation.

We have long admired the initiatives undertaken by Chairman Paul Rogers and the Subcommittee in the health field and are pleased to participate in this undertaking.

Xonics Incorporated has spent $14 million dollars and several years of research to develop an X-ray system to detect breast cancer without simultaneously inducing harmful radiation. We are pleased to present to the subcommittee information concerning the new XERG X-ray units which are now in the field and in use at radiation levels which give reassurance to women who desire to avail themselves to the newest technologies for detecting breast cancer.

We would like to give some background to set the stage for the medical advancement which our company has achieved and then present some cursory details on the XERG system and its deployment throughout the country. We also wish to advise the committee of the assesment of prominent radiologists concerning this new system.

We are aware that the interest of this subcommittee is broad and we submit details only to exemplify that broad consideration.

Currently in the United States, there are approximately five hundred million medical diagnostic X-rays performed annyally. From this number alone, it is apparent that these procedures represent a key element in diagnostic medicine for the American population. Following the discovery of X-ray, at the turn of the Century, various observors noted that deleterious effects could be observed from excessive exposure to x-radiation. However, it was not until World War II that significant scientific studies were begun to properly begin the task of determining what levels of radiation could cause significant harm to human subjects. Ironically, data gathered following the nuclear explosion over Hiroshima provided some of the earliest and most useful information concerning the subject. In essence, studies conducted in Japan provided nuclear scientists with the level of whole body radiation which is fatal.

Although there are different views of the subject, generally it is safe to say that a population of people exposed to 250 Roentgens (R) of whole body radiation over a period of a few minutes or hours can expect half of that population to die in *approximately six weeks. On the other hand, it is generally accurate to say that a human being (never undergoing any diagnostic test (or therapy) utilizing radiation) living at sea level on this planet will absorb approximately 250 milliroentgens (a milliroentgen (mR) is one-thousandth of a roentgen) whole body radiation from the sun each year. Admittedly, this is a wide range of safe to unsafe radiation exposure, but responsible parties will find it most difficult to criticize diagnostic radiation levels less than those received naturally from the sun each year. Therefore it would seem prudent to orient one's concerns toward attempting to develop diagnostic procedures which expose a patient to less radiation than he might normally receive from the sun annually.*

A word about the mechanism of damage which radiation causes to physiological systems is appropriate. Although a number of scientific studies, most of which are being funded by the Federal Government, are currently under way in an effort to thoroughly elucidate the harmful cumulative effects of low levels of radiation, a major element of concern is the damage which can occur to the amino acids which are attached to the double helix carbon chains which form the nuclear material of cells known as DNA and RNA. Inasmuch as each cell nucleus contains approximately 6 million strands of DNA, with each containing millions more amino acid groups (whose combinations make up the so-called genetic code) the potential for altering adversely these genetic codes through ionizing radiation exists. It is believed that sufficient ionizing radiation applied to the DNA that controls cellular growth can create a chemical structure known as a methyl dimer, whereas, prior to the application of radiation, the two methyl groups which form the dimer after radiation exposure were otherwise juxtaposed but probably disassociated biologically. The creation of this methyl dimer may have the effect of distorting the DNA's cellular growth function and could contribute to a carcinogenic cellular growth pattern.

From the foregoing, it is apparent that there is an absolute need to: (a) fully understand the cause and effect relationship between diagnostic studies employing any levels of radiation and (b) since radiological studies are so critical to the health of the American citizenry, to strive for the lowest possible levels of radiation in the conduction of medical diagnostic studies.

It is well known that the radiation required to produce clinically valuable diagnostic images varies from one type of diagnostic study to another. For example, routine chest X-rays can be produced with radiation from 30 to 50 mR to the chest area. On the other hand, routine mammography, through the use of silver halide film or Xeroradiography, can require as much as 800 to 1,000 mR to the breast for each exposure *made. (As recently as 5 to 8 years ago the same exposure might have required 2,000 to 5,000 mR per exposure). Since a complete mammography examination requires at least 4 exposures (2 of each breast) the total radiation required for a mammographic examination has been (and is) much greater than that required for a routine chest X-ray. (This difference is primarily due to the density of the physiological tissue being examined as well as the type of diagnostic information being sought).*

There are many reasons for conducting radiological examinations of different parts of the body, but a brief discussion of the subject of cancer detection may shed some light on the commercial need for effective low-dosage radiological techniques. Approximately 90,000 women in the United States are diagnosed as having breast cancer annually and approximately one-half of these individuals will die from that disease in the following 5 years; thus the 5-year mortality rate for breast cancer is approximately 50%. Since it takes about 5 years for a breast cancer to grow to sufficient size to be clinically detectable by radiological or other diagnostic techniques, the medical community has postulated, and accepts as a general principle, that earlier detection of breast cancer through more sensitive diagnostic techniques, followed by appropriate treatment, should lead to a lower mortality rate. Much of the prevailing theory on this assumption is based upon the reduction in mortality rate during the past 30 years which has occurred in patients with carcinoma of the cervix following the introduction of the Pap test which is in wide general use in the United States and Europe today.

It takes little imagination to recognize the medical/economical benefits to be derived from the earlier detection and effective treatment of any type of cancer. The costs of medical care, borne by society, not to mention the agony borne by the patient, associated with the often protracted clinical course of patients with terminal cancer can be readily demonstrated. On the other hand, studies conducted at UCLA, and by others, demonstrate that the early detection advantage offered by conventional radiology may be negated by repetitive annual conventional mammography, due to the possible induction of cancer in the patients being screened. Thus, the application of the low-dosage Xonics Electron Radiological Technique (XERG), initially for mammography, was derived from consideration of the foregoing state of understanding regarding these variables.

XERG is a patented silverless electrostatic imaging technique which was invented in the early 1970's and which enjoys a significant advantage over other techniques in that the radiation required to produce a clinical useful X-ray image *is approximately 3 to 4 times* *less* *than any other techniques currently enjoyed. At the present time, XERG mammographic systems are being utilized in some 25 locations around the United States, with entrance radiation per exposure of approximately 150 mR to a typical breast, with approximately half of that amount being absorbed by the breast. This type of improvement in radiation exposure for diagnostic studies is applicable to other areas of the body and appropriate techniques for use of the XERG system in these other areas of the body are being developed and should be introduced to the medical community within the next 2-3 years.*

In conclusion, we believe it may now be evident to this subcommittee that the development of XERG system and clinical deployment of new low-dosage X-ray units in the field has been carried out on a very professional basis, one that has been void of promotional type publicity. But the fact does remain that Xonics Incorporated has developed and placed in the field clinically operative units which are now available to the American public. The low-dosage performance of the XERG systems has been amazingly successful. The opinions of a few radiologists in the field might be of use to the subcommittee. May I mention Doctor Phil Strax of the Guttman Institute in New York, Doctor Saar Porath of Santa Monica Hospital in California, Doctor Gary Shaber of Thomas Jefferson Hospital in Philadelphia, Doctor Luther Brady of Hahnemann Hospital in Philadelphia. We, of course, would be pleased to provide additional information to the subcommittee so that an indepth assessment of the XERG systems in the field could be properly assessed.

Finally we understand that in connection with medical cost containment studies undertaken by the federal government, it has been mistakenly asserted that in order to achieve cost savings pursuit of low-dosage diagnostic X-ray technolohy should be abandon or de-emphasized. Perhaps the facts as we have presented to the committee today of already in the field, low-dosage systems resulting from our industrial undertaking and with no cost to the federal government will be of encouragement to Congress and of course, of particular interest to this subcommittee.

Blue Cross®
Blue Shield®

Blue Cross Association
840 North Lake Shore Drive
Chicago, Illinois 60611
312/329-6000

National Association of Blue Shield Plans
211 East Chicago Avenue
Chicago, Illinois 60611
312/943-8181

July 14, 1978

The Honorable Paul G. Rogers
Chairman, Subcommittee on Health and the
Environment of the Committee on Interstate
and Foreign Commerce
Room 2415
Rayburn House Office Building
Washington, D.C. 20515

Dear Congressman Rogers:

The Blue Cross Association and the Blue Shield Association appreciate the opportunity to present our views on diagnostic x-ray utilization to the oversight hearings before the Subcommittee on Health and the Environment.

As third party payors, the Associations are most interested in providing a quality product to subscribers at a reasonable cost. Keeping abreast of efforts to curtail inappropriate and costly utilization of services is a major concern of our organization and we welcome the opportunity to demonstrate some of the programs we have initiated in support of this effort. Attached are responses to eleven issues specifically addressed by your staff.

Again, we are grateful for the opportunity to share our experiences and our concerns regarding the use of diagnostic medical and dental x-rays, and we would be most pleased to cooperate with your staff in any way we can to provide additional information.

Sincerely,

Walter J. McNerney
President

For consistent interpretation of responses to issues set forth in this document, we have assumed that when questions are asked concerning our reimbursement policies, this means coverage policy rather than methods of payment (rate calculations, rate setting design, etc.).

1) What is Blue Cross Blue Shield's present policy with regard to reimbursement for diagnostic medical and dental x-rays?

Blue Cross and Blue Shield Plans are autonomous local organizations. Each Plan develops its own reimbursement policy consistent within its own operating environment, including requirements of group accounts which are often negotiated between management and labor. Some uniformity is accomplished for national account contracts requiring uniform benefits across several Plan areas. The Associations develop medical policy statements through our national Medical Advisory Committee and this information is disseminated to all Plans as an advisory service. Our National Account contract policy (which Plans will oftentimes apply to local business as well) with respect to x-ray coverage limits payment under Blue Shield contracts (physician services) to:

- services rendered to registered bed patients in a hospital, when such an examination is consistent with the diagnosis or the condition for which the subscriber was admitted; or
- when required as the direct result of an accident and when such examination is performed in a physician's office or outpatient department of a hospital.

Specifically excluded under this policy are miniature x-ray plates, screening procedures, x-ray examination made without film (fluoroscopes), and x-rays not directly related and necessary for periodic physical examinations.

Out-of-hospital diagnostic x-ray coverage can be purchased as an optional benefit under this Blue Shield contract.

Under Blue Cross contracts (hospital payment), x-ray benefits on an inpatient basis will be reimbursed provided that:

- such examinations are consistent with the symptomology and/or diagnosis;
- hospitalization was not primarily for such tests; and
- the services are billed by and payable to the hospital.

Specifically excluded are x-ray exams performed when hospitalization was primarily ordered for convenience purposes. Hospital outpatient department x-ray benefits are available for accident situations and medical emergencies.

Dental x-rays are considered a reimbursable item when performed in connection with a covered service.

These policy statements are applied to National Account business and are intended to curtail the unnecessary use of x-rays without depriving the physician of his professional judgment and further, to discourage the use of dangerous x-ray techniques.

Following are some examples of local policy limitations:

- annual dollar limits per contract or per member for diagnostic x-rays;
- requirements for confirmation of diagnosis before reimbursement of x-rays is authorized;

- payment exclusion for x-rays done in conjunction with periodic health exams;
- payment for x-rays required solely by hospital policy;
- initial treatment [x-rays] must be within three calendar days of traumatic injury;
- x-ray (and lab services) are not payable on the same day as an endoscopic or diagnostic procedure;
- x-rays are subject to audit for diagnostic quality if performed by other than a radiologist or certain specialists in their specialties (e.g., by an orthopedist to examine a fracture).

2) Is Blue Cross Blue Shield aware of any studies which indicate that there is a significant incidence of unnecessary x-rays? Is Blue Cross Blue Shield aware of any studies which indicate there is a health risk from x-rays which should be taken into account when considering x-rays of questionable diagnostic value?

The answer is yes to both issues. A library service is maintained at the national level to screen medical journals and other literature. Where appropriate, we make extensive use of national studies and the input of related experts.

More beneficial to us than national studies, however, are the kinds of utilization analysis activities conducted by local Plans for all covered benefits. Blue Cross and Blue Shield Plans regularly perform this kind of function as one of many account servicing activities.

Pattern analysis permits Plans to monitor utilization frequency both by provider and account group. When unusual utilization patterns are identified, Plans may conduct field investigations, medical records audits and medical consultant review specifically to determine the cause of aberrant utilization. When appropriate, corrective action is taken which ranges from provider education programs to stronger steps including claims denial. Because utilization review is conducted at the local level, Plans are in a unique position to effect behavior changes which are responsive to community needs.

3) Does Blue Cross/Blue Shield have a mechanism for keeping abreast of developments in scientific thinking which may alter the definition of good practice and appropriate care? On whom does Blue Cross/Blue Shield rely for such scientific information?

The national Associations have a long-standing and well-established mechanism for keeping abreast of new medical technology and changes in scientific thinking to the degree necessary to make the claims review process responsive to them. The national Medical Advisory Committee, comprised of five physicians, meets approximately five times per year to review the medical efficacy of new and existing procedures. A broad range of internal and external resources are available to it. Policies or opinions are formulated by this Committee, subject to Board concurrence. If the Board does concur, the information is made available to Plans. In an effort to achieve consistent and current thinking on medical policy matters, the Associations' staff responsible for this area have established a firm and continuous communications link with most specialty societies (a particularly sound relationship is established with the American College of Radiology), the FDA, Medicare, Medicaid, OCHAMPUS, medical schools, the Federal Employee Program Operations office, and other resources as necessary.

In addition the national Associations are involved in several major benefit design projects under contract with government agencies. Specific to this topic of radiology services, we have underway a Cancer Screening Benefit study under contract with the National Cancer Institute. This study included analysis of the most recent clinical evidence surrounding use of x-ray cancer screening, specifically lung and breast. A medical advisory committee and numerous other cancer experts were used in the development of this product.

4) Describe the process by which Blue Cross/Blue Shield decides to make changes in its reimbursement policy, and how it goes about making such changes once a decision has been reached?

Once again, each Blue Cross and/or Blue Shield Plan is an autonomous organization and reimbursement policies for lines of business other than national accounts are handled at the local level. Also coming into play here will be variations of benefit design and reimbursement limitations negotiated between labor and management.

At the national level, reimbursement policy positions are subject to approval by the Board of Directors. Through a standing committee structure of the Boards, policy positions are developed and approved for dissemination to Plans for implementation. This Board Committee structure makes wide use of the special expertise required for the development of coverage. The national account comprehensive benefit contract so developed and maintained, must be made available by all Plans for national account business.

5) Describe how Blue Cross/Blue Shield established its program of second opinions on certain surgical procedures, i.e., what was the impetus for such a program, what was the procedure for approval and implementation of the program, and what is the scope of the present program, (all plans, selected plans, subscriber option, etc.)? What studies are being conducted on the long-range medical efficacy and cost effectiveness of this program?

The second opinion program for elective surgical procedures was established on an experimental basis to determine the cost and quality implications of additional consultation. The programs are voluntary mechanisms. To date, the program is being implemented on an experimental basis by approximately 27 Plans. These programs have not been in existence long enough to have determined their real value. However, we have established a formal research protocol to permit the Plans to combine their experience to accelerate a conclusion. This will focus on two essential determinations: the degree of cost effectiveness as it pertains to subscriber utilization of the program; and, savings resulting from non-confirmed surgeries.

6) Has Blue Cross/Blue Shield initiated any studies of the incidence of unnecessary medical x-rays and their cost (health costs and dollar costs) to Blue Cross/Blue Shield subscribers?

Most Plans conduct utilization review to identify excessive utilization frequency.

We view ourselves as having two roles to perform in encouraging appropriate utilization. First, we create utilization data through a variety of claims screening systems and management information systems. These systems are used to support the utilization review departments in Blue Cross and Blue Shield Plans in examining claims for medical necessity and appropriateness and in performing pattern and profile analysis. For example, our Joint Profile System can display possible duplication within an episode of care as well as the x-ray ordering practices of an entire medical staff. Second, we refer documentation of unusual utilization patterns to professional groups -- internal and external -- who are technically competent to evaluate it and have authority to take appropriate action. Such groups include hospital peer review committees and state and local medical societies.

Many Plans have found the use of utilization data a most effective tool to educate providers and thereby effect changes in practice patterns. In support of provider education, the Associations, with the cooperation of the American Medical Association, have developed a film for use by Plans and professional societies which encourages physicians to consider the cost implications of their medical decisions.

We are seeing evidence that physicians are increasingly interested in understanding the economic implications of their medical decisions and are committed to participate meaningfully in the needed solutions to the health care cost problem.

7) The Bureau of Radiological Health of the Food and Drug Administration has estimated that 30% of all diagnostic x-rays ordered each year in the United States are unnecessary. Is Blue Cross/Blue Shield taking any steps to reduce the incidence of unnecessary x-rays? Are there any steps, similar to steps taken by some insurance carriers with regard to control of unnecessary surgery, that could be taken to control or reduce unnecessary x-rays? Would Blue Cross/Blue Shield be willing to participate in a research development effort with respect to ways to control unnecessary x-rays?

We believe that we are taking steps appropriate to our role as a payor for health care services to reduce excessive utilization of all services, including x-ray. As discussed earlier, Blue Cross and Blue Shield focuses on appropriate data collection and display and circulation of that data to professionals whose responsibility it is to modify practice patterns.

At the national level, the Medical Necessity Program, initiated in April of 1977 by the Blue Shield Association and with the cooperation of the American College of Physicians, the American College of Radiology, and the American College of Surgeons, has helped to disseminate cost and quality consciousness among the medical profession.

Included in this program, to date, are 44 procedures (of which six are radiology) which are considered to be outmoded, redundant when performed in combination with others, unlikely to yield additional information through repetition, or of unproven value, and which should be subject to special review before payment is made. The Medical Necessity Program is an ongoing one, which will continue to identify procedures for inclusion in the above categories. Individual Plans have been encouraged to extend it through local medical groups, and some are doing so. The Health Care Financing Administration has recently adopted, with some modifications, this program for Medicare Parts A and B.

We do not believe that second opinion programs in use for surgery could be appropriately expanded to x-ray. Unlike most surgical procedures, x-ray is a diagnostic tool, and from both a cost and quality standpoint, does not lend itself to additional consultation. While awaiting a decision on the medical necessity of x-rays, the risks to the patient arising from treatment delay may increase. Length of hospital stay is also increased without adequate justification for the added cost.

Finally, with respect to Blue Cross and Blue Shield support for additional research efforts to determine x-ray utilization criteria, the Associations would be pleased to work with Plans to coordinate their resources in such activity.

8) The Environmental Protection Agency has developed guidelines for the use of diagnostic x-rays in Federal health care facilities. Has Blue Cross/Blue Shield examined these guidelines? Would you provide Blue Cross/Blue Shield's reaction to these guidelines, both generally and to each individual guideline. Should similar guidelines be developed and supplied to the non-Federal health sector?

We have reviewed the guidelines developed by the Environmental Protection Agency with respect to the appropriate use of x-ray services in Federal health care facilities. The guidelines appear to address three areas. First they deal with the professional disciplines and expertise required for use of radiology services. Interpreting this section on the whole to mean that only professionally qualified health personnel should be involved in the services, we find this to be consistent with our views. We limit Blue Cross and Blue Shield reimbursement to qualified professionals.

Second, they identify a set of procedures contraindicated on a routine or screening basis. We feel that this too is an approach consistent with that utilized in Blue Cross and Blue Shield Plans.

Third, the guidelines deal with the technical quality and safety of x-ray use. We do not believe that, in general, we have an evaluative role in this area. There are some exceptions. Radiological safety is addressed by hospital staff guidelines, radiology peer review committees, state and Federal regulations, etc. Other organizations such as the Joint Commission on Accreditation of Hospitals and the American College of Radiology have a responsibility for evaluating these guidelines for application to the non-Federal sector.

9 & 10) What is the dollar value of Blue Cross/Blue Shield's reimbursement for x-rays for each of the years from 1973 through 1977, and what is the value of its reimbursement for 1967?

Is it possible to estimate how many individual procedures this entails and if this data is not presently available would it be possible to develop a data system which could track numbers of and costs of procedures?

These data are not collected on an aggregate basis for the entire Blue Cross and Blue Shield population. However, it is captured on a local Plan basis by account in the case of larger national contracts or where needed for rate-making purposes. Some cost and frequency information on diagnostic x-rays for enrollees in the Federal Employee Program (high option subscribers) is, however, maintained on an aggregate basis. This is Blue Cross and Blue Shield's largest national account and represents approximately 7 percent of our total business.

The attached data represent Blue Shield expenditures for x-ray services under the FEP Program. These services may include physician interpretation, technical component, or physician reports on x-rays, or any combination of these. Blue Cross payments to hospitals for x-ray services are considered part of ancillary services and are not separately identifiable from aggregate history files. It would be possible to construct a system to track numbers and individual costs of inpatient x-rays, but this would involve changing hospital billing practices as well as data capture methods and would be very expensive. Our own data needs do not warrant the expense to our subscribers.

It should be pointed out that, although the FEP Program does provide coverage for diagnostic x-ray coverage as a basis benefit to all its subscribers, this is not true of all contracts. Estimates could be made and these data extrapolated for future comparison; however, for the moment we are reporting the data at face value.

It must also be noted that this is not a report of individual procedures performed, but of claims processed. Claims may involve only one x-ray, or a series of x-rays which are reported on a single claim form. When observing utilization experience changes between the years 1967 and 1977, it is important to keep in mind certain factors influencing this change. The Blue Cross and Blue Shield subscriber population base changed dramatically along with administrative techniques, billing practices and other organized programs effecting change. Medical technology has had a tremendous impact in terms of making available a wider range of medical services.

11) Is it possible to derive any information from existing Blue Cross/ Blue Shield data with regard to differences in cost and utilization of x-ray procedures which may exist on a regional or geographical basis?

It is possible to compile utilization data on a regional basis. The Associations' Health Economics Research Department is working at this time with the Health Care Financing Administration to develop a data base which will address regional cost variations on a limited basis. This study can be expanded to include a broader range of services, but only at increased cost.

PAYMENT FOR X-RAY SERVICES UNDER FEP HIGH OPTION PROGRAM

		INPATIENT			OUTPATIENT			TOTAL INPATIENT & OUTPATIENT			% of Total Blue Shield Population Represented by FEP High Option Populatior
		Total Claims	Total $ Paid	Average $ Cost Per Claim	Total Claims	Total $ Paid	Average $ Cost Per Claim	Total Claims	Total $ Paid	Average $ Cost Per Claim	
1977	DIAGNOSTIC	84,952	5,857,737	68.95	1,003,333	33,454,127	33.34	1,088,285	39,311,864	36.12	6.9
	THERAPEUTIC	3,584	481,688	134.40	24,458	2,240,190	91.59	28,042	2,721,878	97.06	
1976	DIAGNOSTIC	94,392	5,805,061	61.50	1,073,335	33,578,800	31.28	1,167,727	39,383,861	33.73	7.0
	THERAPEUTIC	2,759	359,817	130.42	23.101	1.951,560	84.48	25,860	2,311,376	89.38	
1975	DIAGNOSITC	93,426	5,084,328	54.42	1,060,380	30,324,714	28.60	1,153,786	35,409,041	30.69	7.3
	THERAPEUTIC	2,434	305.197	125.39	24,024	1,802.319	75.02	26,458	2,107,515	79.66	
1974	DIAGNOSTIC	85,762	4,050,816	47.23	950,154	24,596,935	25.89	1,036,916	28,647,751	27.65	6.9
	THERAPEUTIC	2,624	360,219	137.28	20,848	1,534,803	73.61	23,472	1,895,021	80.74	
1973	DIAGNOSTIC	84,918	3,679,421	43.32	844,695	20,669,924	24.47	929,613	24,349,345	26.19	6.7
	THERAPEUTIC	1,406	165,920	118.00	16,489	1,160,454	70.38	17,895	1,326,374	74.12	
1967	DIAGNOSTIC	------ Combined (Only Figures Available)						254,542	5,223,540	20.52	6.9
	THERAPEUTIC										

[Whereupon, at 4:35 p.m., the subcommittee adjourned.]

○